THE RATIONALE OF THE BLOOD
SEDIMENTATION RATE

By R. G. McFARLANE, M.D.

Clinical Pathologist, Radcliffe Infirmary, Oxford

AND J. R. O'BRIEN, B.M., B.CH.

Graduate Assistant in Clinical Pathology, Radcliffe Infirmary, Oxford.

OBJECTIVE evidence of disease is always sought by the clinician during the investigation of his cases. In particular, he must have data related in some quantitative way to a disease process if he is to assess its severity and rate of change. Such information is often obtained by judgement, but a strong tendency in modern medicine is to measure whatever is measureable so that the numerical results may be compared with greater ease and accuracy than is possible with clinical impressions. In some instances, however, what may be gained in technical precision by these means may be lost in practical value. Figures, as such, are meaningless, but their mere suggestion of accuracy may have an hypnotic effect that obscures the fact that their significance must be judged by the clinician with as much care as any other information relating to his patient. It is their interpretation into terms of physiology or pathology which is of ultimate importance. Above all, they may be positively misleading unless the error of the method which produced them is known.

These preliminary remarks apply with some force to the subject of blood sedimentation. Some estimations, such as blood sugar determination, reflect with relative specificity a known metabolic function in which disturbing factors can be controlled to a considerable extent. Others, such as taking the patient's temperature or counting his white cells, give results that are affected by a wide range of conditions, and it is to this latter group that the estimation of the sedimentation rate belongs. This lack of specificity does not diminish the value of such information. A raised sedimentation rate, for instance, has roughly the same general significance as pyrexia or a leucocytosis, although all three are, of course, independent of each other. They indicate that there is probably something organically wrong with the patient, and further investigation is required to determine the nature of the underlying abnormality. Repeated estimations may give valuable indications of the trend of a disease and assist in the control of treatment. In this connexion, it is strange that, whereas there has been little dispute as to the value of

temperature charts or leucocyte counts, opinions on the sedimentation rate as an index of ill health have differed to such a marked degree that the subject is now surrounded by confusion and complexity. The reasons for this confusion probably lie in the nature of the test itself. In practice, the rate of fall of red cells in plasma can be measured with considerable precision, and with the simplest of apparatus. The process lends itself, however, to endless variations of technique and refinements, or elaborations of recording. Many workers have developed their own methods in this way and, spurred by the enthusiasm of proprietorship, have claimed a significance for their results which is hardly justified.

As regards theory, those with a taste for physics and applied mathematics have found the subject attractive. In consequence, there is now a formidable mathematical literature on blood sedimentation, of undoubted academic elegance but of doubtful practical value at the moment.

Because of these advanced extremes of theory and practice, the average clinician cannot easily see the value of the estimation in its proper perspective. Too often, after failing to reconcile the claims of the enthusiast with the discrepancies of his own routine results, he has tended to dismiss the whole subject as being more bother than it is worth. If he understood for himself the factors involved in sedimentation, and appreciated the extent of present ignorance of the fundamental process, part of his difficulty might be resolved. He would, at least, know the disturbing factors liable to influence his results, and appreciate the extent to which he can rely upon them. It is our purpose to discuss these underlying principles from this point of view.

HISTORICAL SURVEY

Variations in the rate of sinking of red cells in blood have been noticed for centuries. The Greeks based a theory of disease on the separation into layers of blood collected from ill patients during the process of phlebotomy, a separation obviously due to the rapid sedimentation of the cells before clotting occurred. Four layers or humors were described. A dark clot (melancholic) was seen at the bottom with oxygenated red cells (sanguine) on top, whilst a fibrin clot (phlegmatic) formed in the supernatant serum (choleric). Since this separation occurred only in disease it was not unnatural that the four humors should be thought to be the cause rather than the effect, and the practice of phlebotomy to rid the body of these elements of disease was the result of this belief.

A more scientific approach to the subject developed in the 18th century. Hewson, in 1772, was apparently the first to recognize that it was an increased sedimentation rate that produced the buffy coat (fibrin clot) seen in illness, whilst John Hunter appreciated that rapid sedimentation was associated with a granularity of the blood, thus foreshadowing a recognition of the importance of rouleaux formation. Rouleaux themselves

were described by Lister and Hodgkin in 1827; they saw the red cells "apply themselves to each other by their broad surfaces, and form piles", like a pile of coins. These rouleaux were thought by Lister (1857) to be due to an increased stickiness of the cells, and by Norris (1869) to the action of surface tension.

The first practical application of the sedimentation phenomenon as an index of disease was by Fahræus in 1921. He kept blood permanently fluid by the addition of an anticoagulant, and with a simple technique established the range of the normal limits and the variations found in disease. Since this date a vast amount of work has been devoted to the subject; for example, in 1938 alone, at least 129 papers were published on sedimentation. But the words of Denis writing in 1838 on this problem remain essentially true to-day: "Mais autant d'explorateurs, autant d'opinions. Un tel état d'incertitude sur un sujet qui pique si vivement la curiosité . . ."

THE MECHANICS OF SEDIMENTATION

The rate at which red cells sink in plasma is controlled by a series of factors which are familiar from ordinary experience. All objects heavier than their own volume of a liquid will sink in that liquid, and since 1 cubic centimetre of packed red cells weighs about 1.09 gm., whereas a similar volume of plasma weighs only 1.03 gm., red cells will naturally sink in plasma. The speed of the fall will depend upon this weight difference on the one hand, and the resistance offered by the plasma on the other. This resistance increases with an increase in the speed of fall, so that for the constant weight difference between cells and plasma, the individual cells increase the speed of their fall until the resistance offered by the plasma equals the downward force; thereafter they fall at a constant speed. Now the larger a particle the more resistance it meets in its fall, but it will also have a greater weight. The resistance is proportional to its diameter, but its weight is proportional to the cube of its diameter. For example, a sphere twice the diameter of another will meet twice the resistance, but as its weight will be eight times that of the smaller sphere it will therefore sink considerably faster. This effect is familiar; fine grains of sand sink slowly in water; pebbles sink fast. In theory the viscosity of the plasma will affect the rate of fall, but in practice any slowing due to an increase in viscosity is masked by an increased sedimentation rate due to other causes.

In blood, great variations in the size of the falling particles occur. If the red cells remain discrete, they fall slowly, but in certain cases they clump together to form rouleaux in which hundreds or even thousands of cells are packed into a solid mass. The larger these masses are the faster they will fall, and it is their size which largely determines the blood sedimentation rate. These factors are expressed in a mathematical formula known as

Stokes's Law,* which is usually the starting point for discussions on the mechanics of sedimentation. It applies, however, only to small single spheres falling relatively slowly in a large volume of fluid.

An important complication in its application is the existence in blood of large numbers of sinking particles in a relatively small volume of fluid. For every cell that falls, an equal volume of plasma must rise, so that the cells in the neighbourhood will have to fall through an upward current of fluid, and in consequence their rate will be reduced. The larger the number of cells in a given volume of blood the greater will be this retarding effect, a factor that has considerable importance in view of the varying red cell counts in disease.

Rouleaux formation.—It is the formation of rouleaux which is the major factor in sedimentation, and which is the actual index of abnormality; the rate of sinking is merely a simple, if sometimes inexact, measure of their size. The red cells in blood normally remain separate, despite the fact that in the vascular system, and during manipulation of blood samples in the laboratory, frequent collisions must occur. It is clearly of basic physiological importance that such contacts do not result in adhesion, but little is known of the factors concerned in keeping the cells apart. In certain conditions the red cells can become arranged in regular columns, or rouleaux, and these in turn may adhere to each other to form large masses. The process is easily reversible, the formations being broken up by shaking, or by simple dilution of the plasma with a solution of an electrolyte, such as sodium chloride or citrate.

Many different hypotheses have been devised to explain this peculiar loose adhesion of the cells. It was thought that, normally, the electric charge carried by each cell was the main repulsive force keeping them apart, and that alterations in the electrical state of the plasma might reduce this charge, allowing them to come together. No evidence, however, of such a change can be demonstrated in cells forming rouleaux, as against cells remaining discrete. It has been suggested that a change in the red cell surface, or in the envelope of the absorbed plasma protein by which it is presumably invested, might occur so that the red cells become "sticky". This at once raises the problem of what this "stickiness" really is, a question that is too obscure to be dealt with adequately here. In any case, it is a very different sort of stickiness from that which glues the cells together at their first point of contact in true agglutination. In rouleaux formation the cells slide

---

$$V = \frac{2r^2 \, (s_1 - s_2) \, g}{9\eta}$$

*

V = sedimentation rate.

s_1 = specific gravity of particle.

g = gravity

        (981 dynes).

r = radius of particle.

s_2 = specific gravity of fluid.

η = viscosity.

easily over each other to form columns, and separate readily if the physical conditions are altered. It is attraction rather than fusion that keeps them together, although why this attraction should not operate in normal blood cannot, at present, be explained. Surface tension undoubtedly plays an important part in the orientation of the cells. Two cells that make, and for some reason maintain, contact, will by the operation of surface tensional forces tend to slide over each other until their combined surface area is as small as possible, until they are in fact orientated face to face as the beginning of a rouleau. This fact was recognized nearly eighty years ago by Norris (1869), who showed that small discs of cork floating on water formed perfect columns by the operation of surface tension.

The cause of rouleaux formation seems to exist in the plasma surrounding the red cells rather than in the cells themselves. If the cells from a blood sample showing excessive rouleaux formation are washed free from their plasma, they will show no such activity if suspended in normal plasma of the appropriate blood group. The cells from normal blood, however, will form rouleaux if added to the abnormal plasma. No specific substance, analogous to an agglutinin, can be demonstrated in such abnormal plasma, and nothing can be shown to be used up in the process of forming rouleaux; in fact, the abnormality seems to be, not so much the presence of an active substance as the lack of the normal ability of the plasma to keep the red cells apart, an ability which depends upon a particular physical state. In this connexion it may be said that it is, perhaps, unfortunate that in many discussions on sedimentation the term "rouleaux-forming principle" is used, which, however convenient, suggests the existence of a specific substance.

Nevertheless, certain alterations in the constitution of the plasma can be shown to be associated with its tendency to form red cells into rouleaux. An increase in fibrinogen frequently occurs in the inflammatory conditions which are also likely to result in an increased sedimentation rate; and for some time the fibrinogen level was regarded as being the main controlling factor. In some cases, however, there may be a great increase in sedimentation rate without a significant rise in the blood fibrinogen. Recent experimental work has shown that, whilst the addition of fibrinogen undoubtedly increases rouleaux formation, the same result can be achieved by increasing the globulin, or by reducing the albumin content of the plasma. The conclusion seems to be that the tendency of any particular plasma sample to form rouleaux is determined by the balance of "active" against "inhibitory" proteins, fibrinogen and euglobulin being the most active, and an albumin fraction (globoglycoid) and nucleoprotein being the most inhibitory, the other fractions being intermediate or neutral in action (Gordon and Wardley, 1943).

The normal plasma proteins are not the only ones that influence the reaction. In myelomatosis, for instance, an abnormal protein may occur

in the plasma, and its presence is associated with extremely active rouleaux formation and a great increase in viscosity. Despite the latter, sedimentation is rapid, possibly faster than in any other condition. Experimentally it has been found that a number of substances, including gelatin, nucleic acid and hyaluronic acid, all increase the sedimentation rate, although what physical characteristics they have in common with each other and with the plasma protein accelerators is not clear. It may therefore be said that certain alterations in the balance of plasma proteins will result in a physical state in which red cells are liable to form into rouleaux. Such alterations, particularly an increase in fibrinogen and euglobulin, are liable to occur in any condition involving infection or destruction of tissue.

TECHNICAL FACTORS

It has already been shown that the ultimate cause of rapid sedimentation is an abnormality of the plasma induced by disease, and it is only as a measure of this abnormality that the sedimentation rate has practical value. Certain factors are liable to disturb this relationship, however, and these must be considered now. They may be extrinsic, due to variations in the technique of the estimation, or intrinsic, due to alterations in the number, shape or size of the red cells.

Sedimentation rate is usually measured in a blood sample kept fluid by the addition of an anticoagulant, and contained in a relatively long, narrow, graduated glass tube. Therefore the factors to be considered are the effects of the anticoagulant, the age of the blood sample, temperature, the length, bore and inclination of the tube, and the method of recording the rate of fall of the red cells.

The *anticoagulants* commonly used are heparin; a mixture of ammonium and potassium oxalate; and sodium citrate in a 3.8 per cent. solution. Salts such as sodium citrate or potassium oxalate should not be added in solid form to blood, since they increase the osmotic pressure of the plasma, thus causing shrinking and crenation of the red cells which interfere with rouleaux formation. Heparin has no apparent effect in this way and can be added directly to the blood. A mixture of ammonium and potassium oxalates, in the right proportions, results in no distortion of the red cells, since the ammonium group tends to increase the red cell size, being diffusible, thus balancing the shrinking effect of the potassium oxalate. Heparin and the oxalates as such are said to have no effect on sedimentation. The addition of isotonic citrate solution is commonly used, however, and this practice introduces the complicating effect of dilution. Dilution of the plasma reduces its rouleaux-forming activity, thus slowing the sedimentation rate of cells suspended in it, although this is to a small extent off-set by the reduction in red cell concentration that follows. The effect is not even a constant one, since in normal blood there will be less plasma and

more red cells in a given volume than in the blood from an anæmic patient, although the same volume of citrate solution is added to each.

It is a well-established fact that the sedimentation of the blood remains constant for at least two hours after withdrawal from the patient and no great change in rate occurs within four hours. After this time the rate of sedimentation decreases markedly, although the degree of slowing varies somewhat for different anticoagulants and temperatures. The normal variations of laboratory temperature fortunately have little effect on the rate of sedimentation, although results measured in a hot room in summer and a cold room in winter would not be strictly comparable. Nichols (1941) records that the sedimentation rate of the same blood at 38°C., 26°C. and 6°C. was respectively 29 mm., 22 mm. and 3 mm. per hour.

The effect of the *length of the sedimentation tube* on the final result depends upon the method used for recording the rate of fall. In all methods, the increase in length of the clear column of plasma that appears above the red cells is measured, this representing the distance traversed by the slowest moving cells from the uppermost layer of the original blood. If the length of the plasma column is recorded at short intervals and plotted against time, a curve is obtained that has three definite parts. First there is a period of about 15 minutes during which comparatively little fall takes place, so that the curve is relatively flat. During this time, often called the "period of aggregation", rouleaux are in the process of formation. When these have formed, more rapid sedimentation occurs at an approximately constant rate, the curve becoming steeper and nearly linear. The duration of this linear fall, called the "period of free fall", is determined by the length of the tube. There follows a slowing of the rate by the increasing packing of cells at the bottom of the column, until finally movement ceases. These effects are illustrated by the curves derived from blood samples with slow, medium and rapid sedimentation rates, shown in figure 1.

Methods of recording sedimentation rate.—From figure 1 it is clear that there are at least three ways of recording the sedimentation rate. The time necessary for the cells to fall an arbitrary distance may be measured. This has the disadvantage that with slow rates it may take many hours before the cells have fallen the given distance.

The second method consists in measuring the distance fallen at the end of an arbitrary time, e.g., 1 hour. Clearly this is less time-consuming, but ignores the fact that the rate of fall is not constant. Thus, in the fast sedimenting blood in figure 1 the maximal fall and packing were almost complete in half an hour. The period of aggregation rarely takes much more than a quarter of an hour, and so the fall at the end of an hour would bear a close relation to the fastest rate of fall, provided that the slowing effect of packing has not begun by that time. It is with this method of recording that the length of tube assumes great importance. If the tube is sufficiently long, then the packing of cells on the bottom can be ignored, and the period of

free fall is very long in relation to the period of aggregation. In practice, with fast sedimenting blood the slowing effect of packing in tubes up to 200 mm. long will occur within an hour. Thus the advantage of a long period of free fall must be balanced against the disadvantage of the larger volume of blood needed.
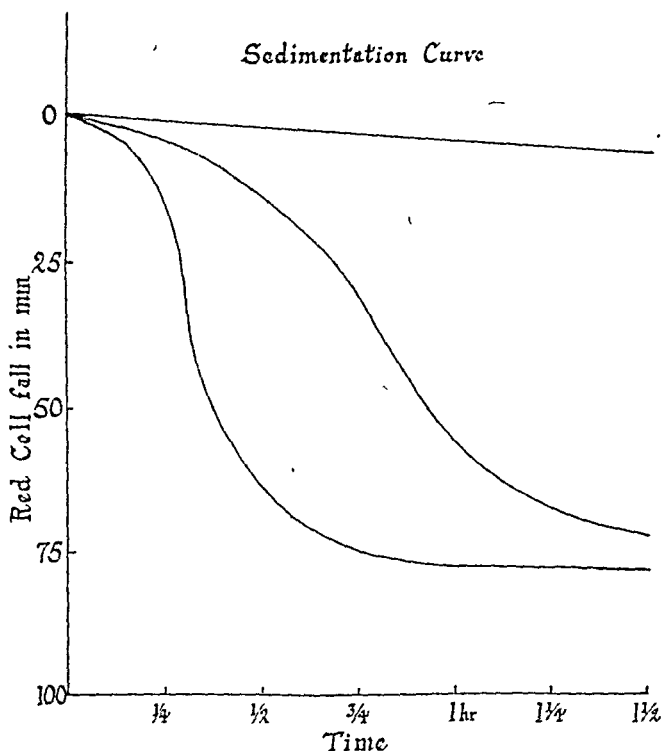

FIG. 1.—Curves of the observed fall of red cells against time. Whole blood, rendered incoagulable was obtained from three patients, one with a low sedimentation rate and two with high rates.

In the third method the periods of aggregation and of packing are avoided, and the maximal rate of fall alone is measured. This last method is scientifically the most accurate, but it is for the clinician to decide if the increased labour of making readings at five-minute intervals, constructing a graph and working out the maximal fall per minute, is justified by a proportional increase in the clinical value of the observation. A further difficulty in all methods when there is gross anæmia is that the rouleaux fall with varying speeds, so that the demarcation between the cells and plasma, which in slow rates is normally a sharp line, may become considerably blurred.

Theoretically the tube should be so wide that the walls play a negligible part in retarding the fall of the cells. If the tube is narrower than 2 mm.

in diameter then it is possible for rouleaux to settle in such a way that a wedge forms right across the tube, preventing further sedimentation. The results of this phenomenon are obvious, as the red cells beneath the obstruction will continue to sink and a second layer of red cells with clear plasma above will form. Temporary blockage may occur which will be shown only by a slowing of the final sedimentation rate.

It is important that the tube used in the test be kept quite vertical. Under these conditions the red cells in falling must displace plasma upwards, so that succeeding red cells fall through an upward current of plasma. If, however, the tube is on a slant, then the cells fall vertically until they approach the lower side of the tube and then slide down the inclined plane. Thus a clear layer of plasma is left under the upper side of the tube which flows upwards without exerting a retarding effect upon the red cells; consequently, tipping the tube will cause an increase in the rate of sedimentation.

Since it is known that the sedimentation rate largely depends upon the size of the rouleaux, it is important to start each observation with the cells separated from one another to the same extent. It is impossible to observe whether after any manipulation the cells are discrete or are still stuck together, as rouleaux formation begins immediately blood is withdrawn from the body. Nichols (1941) found that to get highly consistent results it was necessary to shake the blood at 600 vibrations a minute for fifteen minutes, and even then he suspects that rouleaux may form in the agitated blood. Shaking vigorously by hand for two or three minutes will give results on the same sample of blood that do not differ by more than 2 mm. either way when the total fall is 30 mm. in an hour.

"CORRECTION" FOR ANÆMIA

The most important intrinsic factor disturbing the sedimentation rate is the varying degree of anæmia met with in clinical practice. It has already been pointed out that a reduction in the number of red cells in a given volume of plasma will increase the rate at which they fall, and in practice it is usual to find that in cases of acute anæmia uncomplicated by other disease the sedimentation rate is considerably increased. Since this effect obscures the significance of a raised sedimentation rate in any anæmic patient, many attempts have been made to assess what proportion of an increased rate is due to anæmia alone, so that the additional effect of disease, if any, can be revealed.

Wintrobe (1936) studied the effect of anæmia experimentally by taking blood from normal people only, and diluting it with increasing amounts of its own plasma. The sedimentation rate of the mixtures increased in proportion to the decrease in the red cell count, estimated in this case by the volume of packed cells. He was thus able to construct a curve relating

this artificial anæmia to the varying sedimentation rates observed, shown by the thick line in figure 2. By the mathematical analysis of this curve he constructed a series of others, roughly parallel to the first, represented by the fine lines in figure 2, which he argued would represent the effect of

CHART FOR CORRECTING SEDIMENTATION RATE FOR VARIATIONS RESULTING FROM DIFFERENCES IN THE CONCENTRATION OF RED CORPUSCLES AS MEASURED BY VOLUME OF PACKED RED CELLS
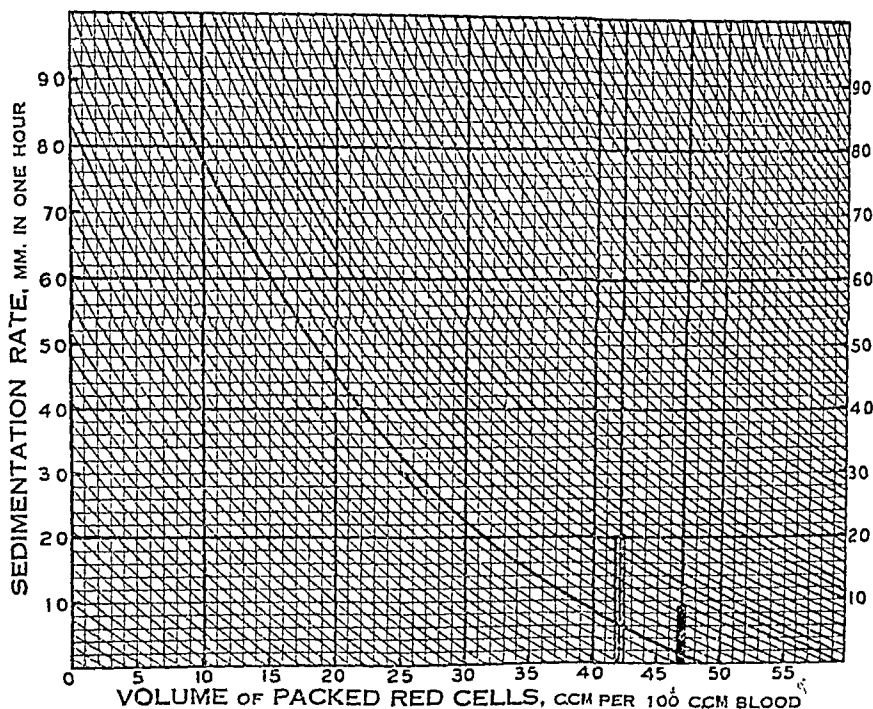

FIG. 2.—Wintrobe's correction chart.

anæmia on abnormal blood samples. He proposed that these curves could be used to predict what the sedimentation rate of a particular blood sample would have been had there been no anæmia. To use the chart the sedimentation rate and packed cell volume of the particular sample are estimated. The intersection of the coordinates of these two values on the chart will fall on or near one of the curves, which is then followed down to its point of intersection with the vertical line corresponding to the normal packed cell volume, this being 42 per cent. in women and 47 per cent. in men. The "corrected" sedimentation rate is then represented by the height of this point above the base line. .

In actual practice it is found that in some cases of chronic anæmia with low packed cell volumes the sedimentation rate is comparatively low, so

that on Wintrobe's chart one of the curves to the left of the thick curved line has to be used. Since these cut the base line before the normal packed cell volume is reached, "negative" corrected values would be obtained. Such a result is due to the obvious fallacy of assuming that the sedimentation rate of all samples of blood will be affected to the same extent by anæmia. If, in fact, Wintrobe's experiment is repeated using a series of blood samples from patients with a wide range of sedimentation rates, a significantly different series of curves is obtained. The results of an actual experiment, which are similar to those of Whitby and Hynes (1938), are illustrated in figure 3. It will be seen that the higher the sedimentation rate at a normal packed cell volume, the greater is the effect of artificial anæmia, as the curves tend to diverge from one another during the initial stages of dilution.

It also will be observed that negative values cannot be obtained, but that, since the curves tend to converge towards the top left-hand corner of the chart, it is difficult to separate the effect of extreme anæmia from the additional effect of disease. This complication is due to the limitation of very rapid sedimentation by the packing of cells at the bottom of the comparatively short tubes used, the point at which this occurs being indicated by the diagonal straight
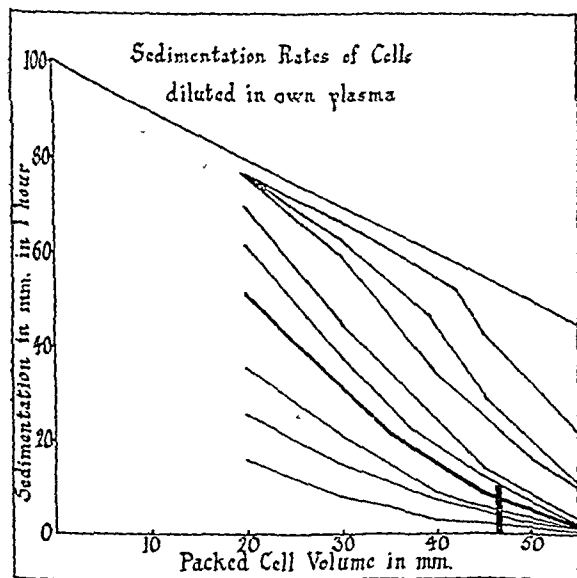
FIG. 3.—Curves showing the effect of diminishing packed cell volumes on sedimentation rates. Each curve represents the sedimentation rates of a series of mixtures of red cells and plasma derived from a particular blood sample.

line in figure 3. This packing effect could be avoided by using a much longer tube, which is extravagant of blood, or by the method of recording the maximum rate of sedimentation, rather than the fall after 1 hour. Some of these difficulties are eliminated by the method of reconstituting the blood to a normal packed cell volume, which is achieved by centrifuging, removing the required amount of plasma, and remixing. It is assumed that such treatment has no serious disturbing effect on the subsequent sedimentation of the blood, other than the removal of the factor of anæmia; and it would

seem to be an ideal method of eliminating that variable. As has already been mentioned, in certain cases of chronic anæmia the sedimentation rate is comparatively low despite the low packed cell volume. Blood from such patients, when reconstituted to a normal packed cell volume, sediments with abnormal slowness, and it appears that in long-standing anæmia there is a natural compensation for the tendency of anæmic blood to sediment quickly; this compensation is brought about by a reducton below normal of the capacity of the plasma to form rouleaux. If this is so, attempts at correction for anæmia may be misleading, since the standardization of red cell concentration cannot eliminate the varying degree of compensation which may occur in anæmia. It can never be decided whether a raised sedimentation rate in an anæmic patient is due solely to the effect of anæmia for which he has failed to compensate, or is due to the effect of disease, despite compensation for the anæmia.

The last factor to be considered is one that affects the red cells themselves. The regular columns characteristic of rouleaux can only form properly if the cells are discs of approximately the same size. In certain conditions there are great variations in the size of the red cells, particularly so in *pernicious anæmia* and other *liver factor deficiencies*. It can be shown that normal cells will sediment more rapidly in the plasma of such cases than the patient's own cells, suggesting that the abnormalities of the red cells prevent their proper aggregation. Variations in the shape of the cells may have similar effects. In acholuric jaundice the cells tend to be spherical rather than discoid, and in sickle-cell anæmia there are great variations in the shape and size; and in both these conditions rouleaux will form with difficulty. A similar change in the cells of blood stored for a long period may explain the loss of sedimenting power seen in such samples.

References

Denis, P. S. (1838): quoted by Fahræus (1928) *Physiol. Rev.*, **9**, 241.
Fahræus, R. (1921): *Acta. med. Scand.*, **55**, 1.
Gordon, C. M., and Wardley, J. R. (1943): *Biochem. J.*, **37**, 393.
Hewson, W. (1772): Works ed. by Gulliver, London, 1846, 1.
Hunter, J. (1835): Works ed. by Palmer, London, **I**, 235.
Lister, J. (1857): *Phil. Trans. roy. Soc.*, **148**, 645.
—— and Hodgkin, T. (1827): *Phil. Mag.*, **2**, 130.
Nichols, R. E. (1941): *J. lab. clin. Med.*, **27**, 1569.
—— (1942): *Ibid.*, **28**, 75.
Norris, R. (1869): *Proc. roy. Soc.*, **17**, 429.
Wintrobe, M. M. (1936): *Internat. Clin.*, (46 ser.) **2**, 34.
Whitby, L. E. H., and Hynes, M. (1938): *Lancet*, ii, 249.

THE BLOOD SEDIMENTATION RATE: A CRITICAL CLINICAL SURVEY

By L. J. DAVIS, M.D., F.R.C.P., F.R.F.P.S.G.

Muirhead Professor of Medicine, University of Glasgow; Physician, Glasgow Royal Infirmary.

NOTWITHSTANDING the widespread employment of the blood sedimentation rate since its introduction as a laboratory test by Fahræus a quarter of a century ago, its status in clinical medicine continues to provoke controversy. Much of this misunderstanding arises, on the one hand, from perfunctoriness in the performance of the test, whilst, on the other hand, failure to appreciate its limitations and the uncritical adoption of technical refinements have tended to invest it with a spurious accuracy and fallacious specificity which have redounded to its discredit. This tendency is regrettable, since in competent hands the test has proved itself a valuable aid in diagnosis, prognosis and treatment over a wide field of clinical problems. It must be emphasized, however, in view of the nonspecific nature of the test and of its inherent limitations, that in no sense can it be regarded as a substitute for clinical proficiency or for established laboratory aids. But when it is an alteration in an ancillary capacity and its interpretation is based on sorying mechanism of sedimen all the aspects of an individual case, it

2) In the case of correction charts their

freqce the relation between the sedimentation trouble incurred.

t linear, and a chart is strictly valid only for a

limentation rate and the same initial red cell concentr

nstruction of the chart. Furthermore, a chart is applicable om

Altsed in its construction.   plications

of (3) Most of the data upon which the correction doctrine is based ha tain

the btained from observations on artificial anæmias produced by the dilution of bh

of ith plasma, but conclusions drawn from such experiments are open to the obje .

of ion that they are not necessarily applicable to clinical conditions. Indeed, it is

of laimed that clinical anæmia *per se* does not in fact accelerate sedimentation to the

xtent that dilution experiments suggest, and that its effect is inconstant and may

ary with the type of anæmia present. Attempts at correction may therefore falsify

Fihe result by "over-correction".

in

pha

CHOICE OF METHOD

as

cli Of the several methods of estimating the sedimentation rate it would seem

r that those necessitating readings at frequent intervals, such as the Cutler and the Rourke-Ernstene techniques, are too time-consuming to justify their adoption for routine purposes. Moreover, it appears highly doubtful that any practical advantage is to be gained by their employment. Of the simpler methods based on a single reading after one hour, the older Westergren and the newer Wintrobe procedures are undoubtedly the most popular.

The Wintrobe method has the advantage that the tube employed may also

seem to be an ideal method of eliminating that variable. As has already been mentioned, in certain cases of chronic anæmia the sedimentation rate is comparatively low despite the low packed cell volume. Blood from such patients, when reconstituted to a normal packed cell volume, sediments with abnormal slowness, and it appears that in long-standing anæmia there is a natural compensation for the tendency of anæmic blood to sediment quickly; this compensation is brought about by a reducton below normal of the capacity of the plasma to form rouleaux. If this is so, attempts at correction for anæmia may be misleading, since the standardization of red cell concentration cannot eliminate the varying degree of compensation which may occur in anæmia. It can never be decided whether a raised sedimentation rate in an anæmic patient is due solely to the effect of anæmia for which he has failed to compensate, or is due to the effect of disease, despite compensation for the anæmia.

The last factor to be considered is one that affects the red cells themselves. The regular columns characteristic of rouleaux can only form properly if the cells are discs of approximately the same size. In certain conditions there are great variations in the size of the red cells, particularly so in *pernicious anæmia* and other *liver factor deficiencies*. It can be shown that normal cells will sediment more rapidly in the plasma of such cases than the patient's own cells, suggesting that the abnormalities of the red cell prevent their proper aggregation. Variations in the shape of the cells may have similar effects. In acholuric jaundice the cells tend to be spherical rather than discoid, and in sickle-cell anæmia there are great variations in the shape and size; and in both these conditions rouleaux will form with difficulty. A similar change in the cells of blood stored for a long period may explain the loss of sedimenting power seen in such samples.

References

Denis, P. S. (1838): quoted by Fahræus (1928) *Physiol. Rev.*, **9**, 241.
Fahræus, R. (1921): *Acta. med. Scand.*, **55**, 1.
Gordon, C. M., and Wardley, J. R. (1943): *Biochem. J.*, **37**, 393.
Hewson, W. (1772): Works ed. by Gulliver, London, 1846, 1.
Hunter, J. (1835): Works ed. by Palmer, London, **1**, 235.
Lister, J. (1857): *Phil. Trans. roy. Soc.*, **148**, 645.
—— and Hodgkin, T. (1827): *Phil. Mag.*, **2**, 130.
Nichols, R. E. (1941): *J. lab. clin. Med.*, **27**, 1569.
—— (1942): *Ibid.*, **28**, 75.
Norris, R. (1869): *Proc. roy. Soc.*, **17**, 429.
Wintrobe, M. M. (1936): *Internat. Clin.*, (46 ser.) **2**, 34.
Whitby, L. E. H., and Hynes, M. (1938): *Lancet*, ii, 249.

to a maximum in puberty, after which it slowly decreases until the onset of old age, when it may again rise. It is also recognized that in healthy females the average rate may be nearly double that recorded for males; the accepted Westergren normal range for males being 3 to 5 mm. in one hour, and for females 4 to 7 mm. Probably some 10 per cent. of healthy young girls may give readings slightly higher than normal.

The only known physiological factor causing a marked elevation of the sedimentation rate is pregnancy, the rate beginning to rise at about the tenth week and returning to normal by the third or fourth week of the puerperium. Sedimentation may be affected in some slight degree by menstruation, exercise, digestion, smoking, climatic influences and certain drugs, but these effects are seldom likely to confuse the interpretation of the test.

It should be noted, however, that although a definitely accelerated sedimentation rate is unusual in normal health, apparently it does occur as a rare phenomenon.

Abnormal readings with the Westergren method may be classified as follows:—

Slight abnormality (to be interpreted with caution)	8–15 mm.
Moderate abnormality	15–40 mm.
Considerable abnormality	40–80 mm.
Extreme abnormality	80–110 mm.

With the Wintrobe technique the readings are higher than these for normality and slight abnormality, but lower for moderate and extreme abnormality.

In pathological conditions, for reasons already mentioned, the behaviour of the sedimentation test cannot always be predicted from first principles; consequently its employment in clinical medicine must depend to no small extent upon empiricism. Generally speaking, however, it can be asserted that sedimentation is usually, but not invariably, accelerated in conditions associated with tissue destruction and in infections and toxæmias causing systemic disturbance, the rate being proportional to the extent of the underlying lesion and to the activity of the pathological process.

It may therefore be accepted as a working principle that a raised sedimentation rate is so unusual in health, apart from pregnancy, that it justifies a strong suspicion of an active pathological state. On the other hand, whilst a normal sedimentation rate renders the existence of active disease unlikely, it must not be accepted as conclusive evidence that no such disease is present.

INFECTIONS

The sedimentation rate is usually considerably accelerated in the more severe conditions resulting from microbic invasion, such as pneumonia, acute bronchitis, septicæmia, tuberculosis, syphilis, malaria, kala-azar and

be used as a hæmatocrit after the sedimentation rate has been determined. This is not only a convenience for general hæmatological purposes but facilitates correction for anæmia, which incidentally may be advisable with this technique. Another advantage is that the anticoagulant used is a dry one which enables blood counts to be performed on the same sample of blood as that used for the sedimentation test.

The Westergren method.—Despite these advantages, in my opinion the method of choice for general purposes is that of Westergren. The reasons for this advocacy are as follows.

The length of the Westergren tube is such that a single reading after one hour gives a very fair indication of the velocity of the phase of rapid sedimentation. The shorter Wintrobe tube is inferior in this respect, since packing tends to occur earlier with blood samples having a high sedimentation rate. The anticoagulant used in the Westergren method, namely, a solution of sodium citrate, exerts a retarding effect which, in conjunction with the influence of the longer tube, appears to facilitate the interpretation of the test, for compared with the Wintrobe method it is less sensitive to minor influences and with normal sedimentation the readings are lower, whilst with rapid sedimentation it is more responsive and the readings are considerably higher.

An important advantage of the Westergren method is its reduced susceptibility to the effects of anæmia. Observations made recently in my clinic on cases of moderate and severe anæmia due to peptic ulcer confirmed that with the Westergren technique the sedimentation rates were normal or only slightly higher than normal, whereas the Wintrobe readings were grossly abnormal. It would therefore seem that with the Westergren technique, correction for anæmia is seldom worth the trouble involved. In patients with gross anæmia and slightly or moderately raised sedimentation rates, or with slight or moderate degrees of anæmia and rapid rates, difficulty in interpretation is rare. Difficulty may be encountered when the anæmia is moderate and the sedimentation rate moderately raised, but in such cases the fallacies attendant upon correction scarcely justify much confidence being placed on the results of this procedure. Correction may, however, be of value when there are reasons for believing the sedimentation rate to be retarded by the presence of polycythæmia.

Finally, the Westergren method has the advantages of simplicity in operation, the necessary equipment and materials being cheap and readily obtainable.

PRACTICAL APPLICATIONS OF THE SEDIMENTATION RATE

Before discussing the clinical value of the test it is necessary to consider the variations that may occur in health. It is generally agreed that the sedimentation rate in infancy is extremely low and that it gradually increases

by an abnormal sedimentation rate. In a recent survey of R.A.F. personnel it was claimed that normal sedimentation rates were present in 26 per cent. of a small sputum-positive group.

TUMOURS

Neoplasms exert a variable effect on the sedimentation rate according to their nature, whether simple or malignant, their location and their extent. In general, sedimentation is not significantly affected by simple tumours and cysts, and is frequently unaffected by localized malignant tumours not associated with much tissue destruction, such as early epithelioma and early scirrhous carcinoma; but it is usually definitely abnormal in rapidly proliferating and in ulcerative malignant conditions, even in the early stages. In the later stages, especially if accompanied by skeletal metastases, a grossly abnormal rate is almost invariably found. The test may therefore be of considerable value in assessing the probability of malignant disease in a number of conditions. Thus, in the differentiation of gastric carcinoma from simple gastric ulcer a significantly raised sedimentation rate justifies suspicion of the former condition. It must, of course, be remembered in this connexion that early scirrhous carcinoma may not necessarily be accompanied by rapid sedimentation, whilst anæmia due to hæmorrhage from a simple ulcer may accelerate sedimentation; but, as already noted, with the Westergren technique this effect is seldom gross. Then in the case of a patient suffering from constipation alternating with diarrhœa, normal sedimentation would render unlikely a diagnosis of carcinoma of the colon, or for that matter of tuberculous enteritis. Again in the diagnosis of palpable abdominal tumours, normal sedimentation would suggest a simple tumour or cyst, whereas an elevated rate, in the absence of pregnancy, would point to a malignant tumour, or degeneration, infection or rupture of a simple tumour or cyst.

It has been claimed that a feature peculiar to malignancy is that the blood sample retains its initial sedimentation rate after storage for twenty-four hours, whereas in all other conditions such a delay results in retardation of sedimentation. Recent work, however, has failed to confirm this claim.

In *Hodgkin's disease* and other forms of reticulosis the sedimentation rate may serve as a guide to X-ray therapy, since it is raised during active proliferation but tends to return to normal during phases of inactivity. A rise in the sedimentation rate therefore serves as an indication for further treatment.

CARDIOVASCULAR DISEASE

The sedimentation test is a valuable aid in the management of two common causes of cardiac damage, namely, rheumatism and coronary thrombosis. In both these conditions the sedimentation rate may be regarded as an index of the activity of the pathological process, for in cardiac disorders not accompanied by active disease the rate is seldom accelerated.

the infectious exanthemas. In pertussis, however, it is said to be retarded.

In *acute fevers* the sedimentation rate is commonly normal during the first day or two and may not attain its maximum rate until after the fever begins to subside. The return to normal is gradual and may be slow. In lobar pneumonia, for example, it may be several weeks after the crisis before the rate is normal.

Although the sedimentation test is seldom of value in the diagnosis of acute infections, it may often be helpful in pointing to the development of complications, since in these circumstances it tends to persist at an elevated level or may show a further rise. For this reason the determination of the sedimentation rate at regular intervals throughout the course of an illness such as pneumonia is often worthwhile, although the information obtained may be of no immediate value during the earlier stages of the disease.

In *mild catarrhal infections* sedimentation is commonly normal, but it may be accelerated during the course of the common cold. This is a point of some importance for, if it be overlooked, a fallacious significance may be attributed to rapid sedimentation in a patient suspected of some more serious condition. Generally speaking, in catarrhal inflammation the sedimentation rate is proportional to its extent and severity. Thus, in anterior urethritis it is commonly normal, whereas in posterior urethritis with prostatitis it may be markedly abnormal.

Suppuration is apt to result in a pronounced rise in the sedimentation rate. Examples of such conditions are otitis media, acute sinusitis, suppurative pulmonary conditions, empyema of the gall-bladder and salpingitis. In small localized infections, however, such as chronic apical dental abscesses and tonsillar infections, sedimentation is frequently unaffected. It is also said to be unaffected in the early phase of appendicitis, in the absence of abscess formation or perforation. The test has accordingly been advocated as an aid in the differentiation between *appendicitis* and *salpingitis*. It is also claimed to be of value in the treatment of the latter condition, since the optimal time for operation, when the inflammation becomes quiescent, may be gauged by the return of the sedimentation rate to normal.

Inflammation of serous cavities, as in pleurisy, pericarditis and peritonitis, is practically always accompanied by rapid sedimentation.

The sedimentation rate is usually normal in *ulcerative conditions* if superficial and uncomplicated, as in peptic ulcer, but it may be accelerated if the ulcer is associated with severe inflammatory changes or with malignant changes.

Wounds and *fractures* affect the sedimentation rate according to their degree and extent.

In *chronic pulmonary tuberculosis* and in certain *rheumatic states* the test is widely used as an index of activity, but this important aspect is dealt with elsewhere in this symposium. At the risk of being redundant, however, it must be emphasized that active tuberculosis is not invariably accompanied

MISCELLANEOUS CONDITIONS

In *disorders of the liver* the test is of little practical value as the results are apt to be discordant. This is understandable in view of the widely varying changes that may be produced in the constitution of the plasma. Thus, increased formation of globulin tends to accelerate sedimentation, whereas decreased production of fibrinogen, or retention of bile salts, may retard it.

Likewise, in *diabetes mellitus* and *thyrotoxicosis* the effects are too variable for the test to be of much clinical assistance.

Acute nephritis accelerates the sedimentation rate, which is said to provide an index of the activity of the condition.

The sedimentation rate may occasionally be of value in the differential diagnosis of *gout*, since it is significantly raised during acute attacks, following the remission of which it rapidly returns to normal. There is, however, apparently no direct correlation with the blood uric acid level.

In *blood diseases* sedimentation is frequently abnormal. The effect of anæmia and polycythæmia *per se* has already been discussed, but in diseases such as leukæmia and pernicious anæmia the effect is greater than can be attributed to the degree of anæmia present.

Acute poisoning with substances such as lead, arsenic and alcohol has been shown to cause acceleration of the sedimentation rate.

Psychiatric and neurological disturbances of functional origin do not affect the sedimentation rate but, as might be expected, in neurological conditions associated with tissue destruction, such as malignant tumours and syphilis, the rate is increased.

CONCLUSIONS

Blood sedimentation is a non-specific biological phenomenon, the mechanism of which is not fully understood.

Since the results of the sedimentation test are readily modified by a number of purely technical factors, a standard technique should be rigidly adhered to. For general clinical purposes the original Westergren method is advocated. With this method correction for anæmia is usually unnecessary and may lead to fallacious results.

The interpretation of the test is based on the general proposition that definite acceleration of the sedimentation rate is exceptional in health, with the exception of pregnancy, but is usually present in certain types of organic disease associated with tissue destruction or systemic disturbance. Since exceptions to this maxim occasionally occur, the test should be regarded as an index of probability rather than of actuality.

If these limitations be borne in mind, and the sedimentation rate be interpreted in conjunction with the clinical and other findings in each case, it provides a valuable guide in the diagnosis, prognosis and treatment of many clinical problems.

In *rheumatic carditis* sedimentation is extremely rapid but returns to normal with subsidence of activity. Following *coronary thrombosis* it usually attains a high maximum rate during the second or third week, whilst subsequently, as the infarct heals, it may return to normal or, alternatively, may persist for some time at a constant level slightly above normal. Hence, weekly readings provide valuable information in both these conditions, since, in fact, they reflect the state of the lesion more closely than do the pulse, temperature or leucocyte count. It is a safe general rule in practice to keep the patient in bed until the sedimentation rate returns to normal, or in coronary thrombosis to a constant if slightly elevated rate. It is necessary to point out, however, that there are reasons for believing that in rheumatic carditis the sedimentation rate may in exceptional cases persist at a moderately elevated level for some considerable time after the subsidence of activity.

The foregoing remarks are also largely applicable to *cardiovascular syphilis*, sedimentation being accelerated in untreated cases but returning to normal following successful treatment.

The sedimentation rate is raised in *bacterial endocarditis* but the multiple factors involved in this condition make its interpretation difficult in diagnosis. It may, however, prove of value in assessing the results of penicillin therapy. Further information on this point is clearly desirable.

In evaluating the sedimentation rate in heart disease it is important to appreciate the effect of *congestive failure*, since this retards sedimentation. Indeed, the onset of congestive failure may result in the sedimentation rate falling to normal levels despite the presence of an active or progressive lesion. Therefore in the presence of congestive failure a normal sedimentation rate should be interpreted with caution.

In *hypertensive heart disease* the sedimentation rate is variable, being usually normal in the milder cases, sometimes moderately elevated in the more severe cases and frequently rapid in malignant hypertension. It seems probable that renal impairment may be a determining factor in accelerating sedimentation, whereas congestive failure tends to exert a retarding effect.

Angina of effort usually has no marked effect on sedimentation, although in severe cases moderate acceleration has been recorded. In cases of præcordial pain of doubtful etiology the test may be of value, for a sedimentation rate remaining normal, or only slightly elevated, a week or so after the onset of pain is presumptive evidence against coronary thrombosis. The test may also occasionally help in the evaluation of cardiac murmurs of questionable innocence, since an abnormal sedimentation rate, without other cause, would justify suspicion of active *valvular disease*. The converse, however, obviously does not apply, for although a normal rate in the absence of congestive failure renders active disease unlikely, it would not exclude the possibility of valvular damage from pre-existing organic disease.

METHODS OF ESTIMATING THE BLOOD SEDIMENTATION RATE

By J. M. ALSTON, M.B., Ch.B., M.R.C.P.Ed.

Pathologist, Group Laboratory, Archway Hospital, London.

THE sedimentation rate of red blood corpuscles is a simple determination and several techniques have been employed. Two of these, Westergren's and Wintrobe's, have become the most frequently used in this country. The procedure in these and other techniques is to prevent coagulation of a small amount of whole blood, to fill a narrow tube with a column of measured height and to observe the extent to which the red corpuscles fall in a given time or the time required for them to fall a stated amount. Variations may be caused by differences in the details of making the test, and therefore a careful standardization of handling is required. The different methods give considerably different results which cannot be changed readily into the terms one of another. These are important aspects of the test, since its greatest use is to assist in assessing the progress of a patient's condition from month to month in certain chronic illnesses.

BASIC TECHNICAL POINTS

In all methods the following are important points which should be observed in taking blood and setting up the test:—

(1) Venous blood taken into a syringe is preferable to capillary blood, although the latter is used in some "micro" methods (*vide infra*).

(2) If the limb is constricted to fill a vein, the constriction should be slight or removed as the blood is withdrawn.

(3) The blood and the anticoagulant must be mixed thoroughly and as soon as possible (in the syringe in many methods).

(4) The test should be set up within a few hours of the withdrawal of blood (more exact directions on this point are given in certain methods).

(5) All the glass-ware and needles used in the test must be well washed to prevent contact of antiseptics or other chemicals with the blood.

(6) Hæmolysis of corpuscles falsifies the results.

(7) The bore of the tubes used for observing the sedimentation must be within the limits stated; these tubes must be dry and, during sedimentation, they must be vertical.

(8) Bubbles of air in the column of sedimenting blood must be avoided.

WINTROBE'S METHOD

Five c.cm. of venous blood is collected with a dry syringe and needle and injected into a small bottle which contains 4 mgm. of solid potassium oxalate and 6 mgm. of solid ammonium oxalate. These bottles of "double oxalate" are most easily prepared beforehand by pipetting into the bottles small amounts of solutions of the salts in suitable concentration and sterilizing the bottle in a hot-air oven. The bottle must be shaken for a

BIBLIOGRAPHY

Because of the extensive literature, detailed references have not been given in
the text of this article. Readers desiring further information are referred to the
undermentioned key papers and reviews:—

Apter, L., Hull, E., and Adams, C. C. (1943): "Maintenance of the Sedimentation
Rate as a Test for Malignant Disease". *Amer. J. med. Sci.*, **206**, 169.

Bailey, L. J. (1941): "A Clinical Evaluation of the Sedimentation Test in Tuber-
culous Mental Patients with Particular Reference to the Reliability of Corrected
Sedimentation". *Internat., Clin.* **4**, 53.

Bannick, E. G., Gregg, R. O., and Guernsey, C. M. (1937): "The Erythrocyte
Sedimentation Rate, Adequacy of Simple Test and its Practical Applications
in Clinical Medicine". *J. Amer. med. Ass.*, **109**, 1257.

Benson, L., and Rogers, E. J. (1940): "The Blood Sedimentation Rate in Healthy
Girls". *J. lab. clin. Med.*, **26**, 987.

Bouton, S. M. (1938): "Erythrocyte Sedimentation and Anæmia". *Ibid.*, **23**, 519.

Cutler, J. W. (1932): "The Practical Application of the Blood Sedimentation
Test in General Medicine; Observations Based on Approximately 5,000
Patients over a Period of Six Years". *Amer. J. med. Sci.*, **183**, 643.

—— (1940): "A Standardized Technique for Sedimentation Rate". *J. lab. clin.
Med.*, **26**, 542.

Fahræus, R. (1921): "The Suspension Stability of the Blood". *Acta med. Scand.*,
55, 1.

Gram, H. C. (1929): " The Sedimentation of the Blood Corpuscles in Various
Internal Diseases and the Result of Correction of this Value for the Variations
of Hæmoglobin Percentage". *Ibid.*, **70**, 242.

Haden, R. L. (1942): "The Sedimentation Rate in Gout". *J. lab. clin. Med.*, **27**,
725.

Ham, T. H., and Curtis, F. Y. (1938]: "Sedimentation Rate of Erythrocytes".
Medicine, **17**, 447. (A comprehensive review giving numerous references to
earlier work).

Riseman, J. E. F., and Brown, M. G. (1937): "The Sedimentation Rate in Angina
Pectoris and Coronary Thrombosis". *Amer. J. med. Sci.*, **194**, 392.

Rourke, M. D., and Ernstene, A. C. (1930): "A Method for Correcting the
Erythrocyte Sedimentation Rate for Variations in the Cell Volume Percentage
of Blood". *J. clin. Invest.*, **8**, 545.

Rubin, M. I., Rapoport, M., and Waltz, A. D. (1942): "A Comparison of Routine
Urinalysis, Addis Count and Blood Sedimentation Rate as Criteria of Activity
in Acute Glomerulonephritis". *J. Pediat.*, **20**, 32.

Smith, C. T., Harper, T., and Watson, A. (1935): "Sedimentation Time as an
Aid in Differentiating Acute Appendicitis and Acute Salpingitis". *Amer. J.
med. Sci.*, **189**, 383.

Trenchard, H. J. (1945): " Symptoms of Early Pulmonary Tuberculosis".
Lancet, ii, 842.

Walton, A. C. R. (1933): "The Erythrocyte Sedimentation Test". *Quart. J.
Med.*, **2**, 79.

Westergren, A. (1921): "Studies of the Suspension Stability of the Blood in
Pulmonary Tuberculosis". *Acta med. Scand.*, **54**, 247.

Wintrobe, M. M. (1936): "The Erythrocyte Sedimentation Test". *Internat.
Clin.*, **46**, 34.

—— and Landsberg, J. W. (1935): "A Standardized Technique for the Blood
Sedimentation Test". *Amer. J. med. Sci.*, **189**, 102.

Wise, R. (1942): "The Sedimentation Rate in Hodgkin's Disease". *J. lab. clin.
Med.*, **27**, 1200.

Wood, P. (1936): "The Erythrocyte Sedimentation Rate in Diseases of the
Heart". *Quart. J. Med.*, **5**, 1.

anæmia, the hæmatocrit is centrifuged at 2,500 revolutions per minute after the sedimentation readings for one hour have been noted, and the volume of the packed cells as a percentage of the volume of cells and plasma is thus obtained. It should be noted that, whereas in reading the sedimentation rate the measurement is of the height of the column of plasma (and leucocytes), for the cell volume it is the column of red corpuscles (after centrifuging) that is measured. The use and desirability of correcting the sedimentation rate for anæmia will be mentioned later. A "micro" modification of Wintrobe's method is to puncture the heel or finger and transfer with a capillary pipette 0.6 c.cm. of blood, in successive amounts of 0.1 c.cm., into a bottle containing 0.8 mgm. of solid potassium oxalate and 1.2 mgm. solid ammonium oxalate. With this the hæmatocrit may be filled to the 50 mm. mark.

WESTERGREN'S METHOD

A 1 to 2 c.cm. syringe is one-fifth filled with 3.8 per cent. solution of sodium citrate and then to capacity with venous blood. The blood and citrate solution is then mixed by quickly emptying it into a small tube and shaking. When setting up the test, specimens showing hæmolysis and clots are discarded, and, if these are absent, the solution is again mixed thoroughly. The mixture of blood and citrate is drawn up to 200 mm. in a pipette of 3 mm. bore and 300 mm. long, and the pipette is stood upright in a special stand made by Leitz, or in one which can be improvised; in this stand, each pipette is held vertical between a spring clip above and a small rubber pad below (Schilling, 1929).

The corpuscles usually sink into a column with a well-defined upper edge and the reading is taken at the end of one hour by measuring from the graduations on the pipette, or with a ruler, the height of the column of clear fluid (and leucocytes) above the red corpuscles. The range of result found in healthy men is 1 to 3 mm., and in healthy women 3 to 7 mm.

A simpler form of the test uses blood withdrawn and mixed with 3.8 per cent. sodium citrate, as above, and a piece of ungraduated glass tube 150 mm. long and 3 mm. in bore. This is marked at 100 mm. from one end, well mixed blood and citrate are drawn up to the 100 mm. mark, the end of the tube which has been dipped into the mixture is cleaned and the column of 100 mm. drawn a few millimetres up from the lower end of the tube. The tube is then stood upright in a small, improvised rack or in plasticine on a level surface.

By this method results from 1 to 5 mm. are found in healthy men and women.

When vein puncture is not permissible, blood may be less suitably obtained from the capillary circulation by skin puncture. A convenient way is to take 0.1 c.cm. of 3.8 per cent. sodium citrate solution into a 1 c.cm. pipette and then draw up 0.4 c.cm. of fairly free-flowing blood. The citrate solution and blood are immediately mixed in a tube, and a column of 100 mm. may be set up in either a Westergren tube or the ungraduated tube already mentioned.

LINZENMEIER'S METHOD

This records the sedimentation rate in terms of the time required for a fall of a given extent.

A tube 65 mm. long and 5 mm. wide is marked at 51 mm. from the lower end and at 18 mm. and 24 mm. below the 51 mm. mark; 0.8 c.cm. of blood is drawn up into a 1 c.cm. syringe which contains 0.2 c.cm. of 5 per cent. sodium citrate solution. The

minute after the blood has been put into it, in order to ensure rapid solution of the dry oxalate salts and complete absence of coagulation of the blood. Only 1 c.cm. of blood is required for the sedimentation rate and the remainder is used for counts of corpuscles and platelets and for films. The blood should be used within two hours.

Wintrobe's hæmatocrit, a tube of 2.5 mm. bore, closed at the lower end and graduated in millimetres, is filled to 100 mm.: this is done by drawing up the well-mixed blood in a thin capillary tube which will pass to the bottom of the hæmatocrit, avoiding bubbles of air in the column of blood. The tube is put in a stand which keeps it vertical and which, in its more elaborate forms (fig. 1), has spirit levels and adjustable screw feet. This type of stand is recommended by Whitby and Britton (1946) and can be obtained from Stephen Perkins, 124 Exeter Road, Harrow. The need for keeping the tube vertical is emphasized by the fact that a deviation of 3° from the vertical affects the result.
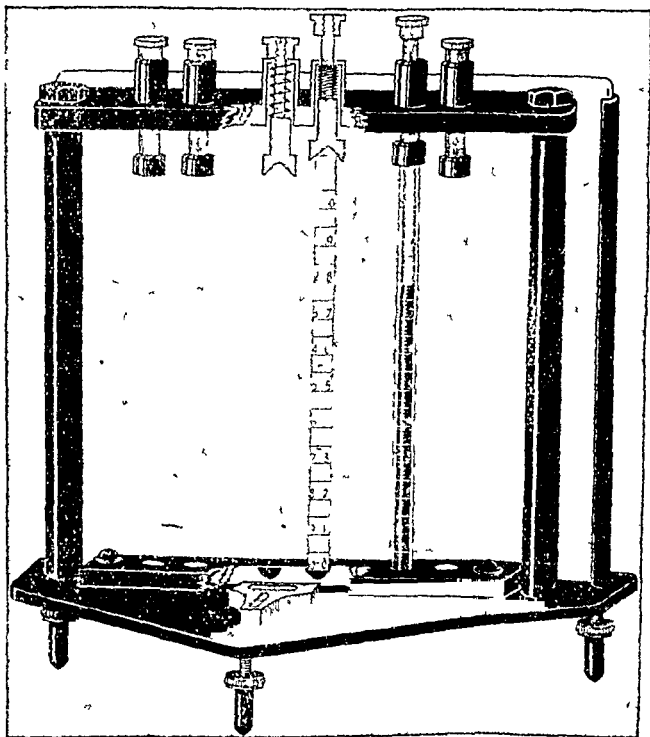
FIG. 1—Stand for holding Wintrobe's tube.

(Fig. 1 and 2 are reproduced from Whitby and Britton's "Disorders of the Blood", 5th edition, 1946. J. & A. Churchill Ltd).

A single reading of sedimentation may be made after one hour, or more frequently if a graph of the course of sedimentation is to be made (*vide infra*). The "rate" in healthy people is as follows:—0 to 6.5 mm. at one hour in 86 per cent. of young men, and 0 to 15 mm. at one hour in 88 per cent. of young women, with an average of 3.7 mm. for men and 9.6 mm. for women. If it is desired to make a "correction" of the sedimentation rate for

TECHNIQUE OF CORRECTION FOR ANÆMIA

I have referred to correction for anæmia. This can be done on the basis of the cell volume already mentioned or the percentage of hæmoglobin. Charts have been prepared from observations with specimens of blood made artificially anæmic by removal of corpuscles. One prepared by Whitby and Hynes (1938) is shown in figure 2. In using it to correct for anæmia, the junction of the lines of the observed sedimentation rate and the observed corpuscular volume is noted; this point will fall in one of the five zones named on the chart which indicate the approximate degree of increase in the rate. If a definite compensated figure is required, the approximate curve is followed down to the point where it cuts the 45 c.cm. thick vertical line (which is the figure of the average corpuscular volume), and the sedimentation rate at that level is called the correction rate.

Methods of correcting for anæmia in this way have been discussed by Gibson (1938). Consideration of these methods emphasizes that sedimentation is governed by many more factors than the number of red corpuscles and, in my view, to attempt to remove this one factor approximately is a false method of simplification. It is better to regard the test as measuring the general condition of many mechanisms of the body. The degree of anæmia of the patient should be known and, if possible, corrected *in vivo;* if the patient's blood cannot return to normal, it is meaningless to correct for it on paper. Every other measure must be taken for restoring health and the test is then a useful indication of the progress of treatment.

USE WITH LEUCOCYTE COUNTS

The sedimentation rate has been used in conjunction with other findings to give a more accurate prognosis in diseases such as tuberculosis. For example, Houghton (1936) adds to his calculations the percentage of lymphocytes, monocytes and polymorphs and the stage of development of these last. He uses the method of von Bonsdorf for assessing the age of polymorphs, and therefore counts the number of separate nuclei in 100 polymorphs, judging as separate those nuclear masses which are connected to others by no more than a thread. Favourable factors in the equation are larger numbers of nuclei (V.B.), higher percentage of lymphocytes (L.), lower percentages of monocytes (M) and polymorphs (P), and low sedimentation rate (S.R.), which he estimates by Westergren's method with a column of 200 mm. The calculation is set out as follows:—

$$V.B. - [S.R. + (P + M - 2L)] = \text{index}.$$

An example in a patient with progressive tuberculosis might be $200 - [40 + (65 + 10 - 50)] = 135$.   The higher the figure the better is the prognosis.

References

Cutler, J. (1926): *Amer. J. med. Sci.,* **171,** 882.
Gibson, H. J. (1938): *Proc. roy. Soc. Med.,* **31,** 309.
Houghton, L. E. (1936): *Brit. med. J.,* ii, 1246.
Schilling, V. (1929): "The Blood Picture," London.
Whitby, L., and Hynes, H. (1938): *Lancet,* ii, 249.
—— and Britton, C. (1946): "Disorders of the Blood", 5th ed., London
Wintrobe, M. (1942): " Clinical Hæmatology", Philadelphia, p. 167.

tube is filled to the 51 mm. mark from the syringe and the tube shaken well and then stood upright. The time is noted at which the red corpuscles settle as far as the 18 mm. mark and, if required, the 24 mm. mark (Schilling, 1929).

In healthy men 18 mm. is reached in 350 to 1500 minutes and in healthy women in 300 to 600 minutes. This method is mentioned because it is on a different principle from Westergren's and Wintrobe's, but it is trouble-some except when pathological work is done day and night.

CUTLER'S METHOD

Cutler has described a method of charting the course of sedimentation by frequent readings.

Into a 5 c.cm. syringe there is aspirated 0.5 c.cm. of 3 per cent. sodium citrate and 4.5 c.cm. of venous blood; they are mixed in the syringe. The needle is then removed and the blood-citrate mixture poured into the sedimentation tube of 5 c.cm. capacity which is graduated in millimetres, each corresponding to one-tenth of a c.cm. volume. The tube is stoppered with a paraffin-coated cork and the solution gently mixed. The record should be begun, after fresh mixing, within ten hours of withdrawal of blood. The tube is set to stand vertically and the height of the column of red corpuscles is measured every 5 minutes for an hour. The readings are plotted on a squared graph paper against the times of recording.
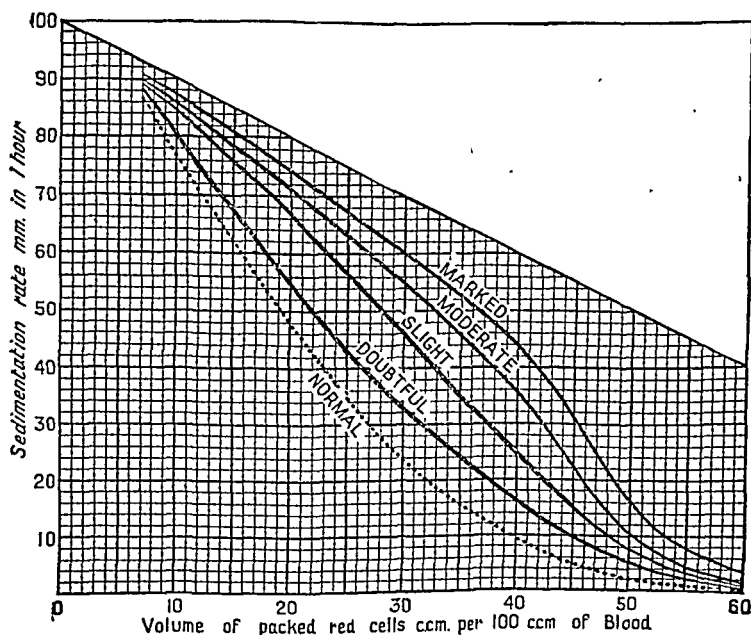

FIG. 2.—Chart for correction of sedimentation rate for anæmia by means of the corpuscular volume.

The figures found after one hour of settling are 2 to 8 mm. for men and 2 to 10 for women. For any final figure, the more steeply the line on the graph falls from the beginning of the observations, the worse the indication. Automatic records can be taken by exposing slowly moving photographic films or plates behind the sedimentation tube so that the difference between the supernatant plasma and the settling corpuscles is seen.

METHODS: WITH SPECIAL REFERENCE TO THE RHEUMATIC DISEASES

The method which I regard as most useful in the rheumatic diseases is the *Spa Hospitals' method* of Collins et al. (1939). This was chosen after three years' experience (some 6000 tests) in which the wide-bore conical centrifuge tube, as used in that method, was employed in parallel with the Wintrobe and Westergren methods. It was then found that the wide-bore tube was most sensitive in showing the slightest indication of an increase in rate. The Wintrobe tube was very little inferior in this respect, but with the Westergren tube, in approximately 5 per cent. of cases, there was a definite "hold-up" of the red cell aggregates for one and sometimes two hours, giving readings within normal limits when the other two methods showed a significantly increased rate. This experience was completely in agreement with that of Rodgers (1945), who attributed much of the recent scepticism concerning the value of the B.S.R. to the continued use of the Westergren tube. The Spa Hospitals' method is standard in the hospitals for rheumatism at Harrogate, Buxton, Droitwich, Bath and elsewhere.

As will be seen later, a strictly normal B.S.R. has a considerable significance in the diagnosis of chronic rheumatism and it is of great importance to use the method which is least liable to record a false normal result, even if it involves the sacrifice of some accuracy in distinguishing between bloods of the most rapid rates, such as long tubes of the Westergren type may afford. It is also to provide a maximum of sensitiveness that we prefer to use undiluted blood, mixed with dry oxalate, rather than to dilute with citrate solution. As the citrate solution mixes only with the plasma, the use of a constant citrate solution:blood ratio results in a very variable dilution of plasma, depending upon the red cell volume. As the packed red cell volume in women with active rheumatoid arthritis is frequently below 30 per cent., whilst in males with gout it may be over 50 per cent., this factor becomes a source of considerable, and easily avoidable, error in the group of diseases dealt with in this article.

Our practice for the past eight years has been to use the wide-bore conical tube of the Spa Hospitals' method in parallel with Wintrobe's tube. This is a check on a rare source of error which has been described by Shackle (1938). For no apparent reason the red cells fail to fall. If the tube is re-shaken sedimentation is satisfactory. By using two tubes in parallel the error can be noted at once from the discrepancy between the readings. My experience is that there is little to choose between the two methods and both are recommended. For use by the general practitioner who wishes the minimum of apparatus the Spa Hospitals' method is ideal.

A supply of conical 5 c.cm. centrifuge tubes graduated in 100 parts by volume is all that is required. These are obtainable from the Scientific Glass-blowing Company. At least 5 c.cm. of blood is taken from a vein and placed in a 1-ounce screw-cap vial or other suitable container, in which dried potassium oxalate (2 mgm. for each c.cm. of blood) has been previously placed. The bottle is then gently inverted

THE BLOOD SEDIMENTATION RATE IN RHEUMATOID ARTHRITIS AND ALLIED CONDITIONS

By H. J. GIBSON, M.D., D.P.H.

Pathologist, Royal National Hospital for Rheumatic Diseases, Bath.

BECAUSE of the few available objective standards by which the physician may assess progress or deterioration, the chronic rheumatic diseases present many problems of diagnosis and management. The temperature shows no reliable relationship to activity as it does in tuberculosis. The pulse rate gives no material assistance. For this reason the blood sedimentation rate (B.S.R.) is of peculiar importance and service in this group of diseases. There is no specific test such as the Wassermann reaction. No causative organism has ever been isolated by which the diseases can be identified etiologically, either by demonstration of the organism or its antibodies. Therefore, for the present, this non-specific test must be employed.

It cannot be too strongly emphasized that the test is non-specific, and when its use in diagnosis is referred to, this refers especially to diagnosis within the rheumatic group. "Chronic rheumatism" is an extremely protean group of diseases which may be simulated by many infections, new growths, organic central nervous lesions, bone diseases and a host of other conditions. Only when the case has been allocated to the rheumatic group with reasonable certainty can the information given by the B.S.R. be of value.

The increased rate of fall of red cells in "arthritis deformans" was noted by Fahræus (1921) in his original monograph and the test was soon widely adopted. Kahlmeter (1926) published the results of a large series of tests in chronic rheumatic cases of all kinds and established the practical usefulness of the test. Recently opinions have been expressed by MacIntosh and Keay (1945), Harkness *et al.* (1946) and others, as to the unreliability of the test in any chronic disease. The former writers were concerned with tuberculosis and the latter did not include any cases of chronic rheumatism in the series upon which they based their conclusions. The fact remains, however, that the test has been employed over a period of more than twenty years as a routine in rheumatic clinics and hospitals in many parts of the world. The results have been closely scrutinized in association with the clinical condition and it has become recognized as a source of valuable information which no other investigation at present affords. No claim is made that it is an index of all plasma abnormalities in rheumatism or other chronic disease. There is evidence from many directions that certain changes in the globulins are not indicated by this test, but their precise significance has yet to be established.

METHODS: WITH SPECIAL REFERENCE TO THE RHEUMATIC DISEASES

The method which I regard as most useful in the rheumatic diseases is the *Spa Hospitals' method* of Collins *et al.* (1939). This was chosen after three years' experience (some 6000 tests) in which the wide-bore conical centrifuge tube, as used in that method, was employed in parallel with the Wintrobe and Westergren methods. It was then found that the wide-bore tube was most sensitive in showing the slightest indication of an increase in rate. The Wintrobe tube was very little inferior in this respect, but with the Westergren tube, in approximately 5 per cent. of cases, there was a definite "hold-up" of the red cell aggregates for one and sometimes two hours, giving readings within normal limits when the other two methods showed a significantly increased rate. This experience was completely in agreement with that of Rodgers (1945), who attributed much of the recent scepticism concerning the value of the B.S.R. to the continued use of the Westergren tube. The Spa Hospitals' method is standard in the hospitals for rheumatism at Harrogate, Buxton, Droitwich, Bath and elsewhere.

As will be seen later, a strictly normal B.S.R. has a considerable significance in the diagnosis of chronic rheumatism and it is of great importance to use the method which is least liable to record a false normal result, even if it involves the sacrifice of some accuracy in distinguishing between bloods of the most rapid rates, such as long tubes of the Westergren type may afford. It is also to provide a maximum of sensitiveness that we prefer to use undiluted blood, mixed with dry oxalate, rather than to dilute with citrate solution. As the citrate solution mixes only with the plasma, the use of a constant citrate solution:blood ratio results in a very variable dilution of plasma, depending upon the red cell volume. As the packed red cell volume in women with active rheumatoid arthritis is frequently below 30 per cent., whilst in males with gout it may be over 50 per cent., this factor becomes a source of considerable, and easily avoidable, error in the group of diseases dealt with in this article.

Our practice for the past eight years has been to use the wide-bore conical tube of the Spa Hospitals' method in parallel with Wintrobe's tube. This is a check on a rare source of error which has been described by Shackle (1938). For no apparent reason the red cells fail to fall. If the tube is re-shaken sedimentation is satisfactory. By using two tubes in parallel the error can be noted at once from the discrepancy between the readings. My experience is that there is little to choose between the two methods and both are recommended. For use by the general practitioner who wishes the minimum of apparatus the Spa Hospitals' method is ideal.

A supply of conical 5 c.cm. centrifuge tubes graduated in 100 parts by volume is all that is required. These are obtainable from the Scientific Glass-blowing Company. At least 5 c.cm. of blood is taken from a vein and placed in a 1-ounce screw-cap vial or other suitable container, in which dried potassium oxalate (2 mgm. for each c.cm. of blood) has been previously placed. The bottle is then gently inverted

to dissolve the oxalate. Wintrobe's mixture of ammonium oxalate 6 parts, potassium oxalate 4 parts, is recommended instead of potassium oxalate alone. The amount of the combined oxalates is the same as with potassium oxalate. The test must be put up within three hours of taking the blood, which is poured into the conical tube up to the 5 c.cm. mark. The tube is then allowed to stand vertically for one hour, when the red cell level is read.

The strictly normal for males is 90 per cent. or more (red cell volume: 1 hour), for females 85 per cent. or more. It may be noted in passing that the estimation of B.S.R. is of great value in general medical and surgical diagnosis, an increased rate indicating a deep-seated tissue-destructive process, and the use of this simple test provides a valuable addition to the practitioner's diagnostic methods.

TABLE I

Blood Sedimentation Rate and Clinical Type.
Percentage of cases in each B.S.R. group.
B.S.R.

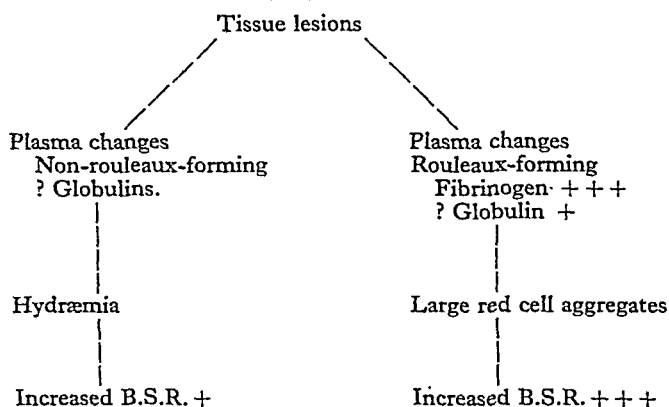| Clinical type	100–90 0–10	89–80 11–20	79–70 21–30	69–60 –40	59–50 –50	49–40 –60	39–30 –70	Red cell vol. per cent. 1 hr. Min. fall 1 hr. (Wintrobe)
Normal ..	55	27	13	5	0	0	0	
Fibrositis ..	55	28	10	7	0	0	0	
Osteo-arthritis . ..	32	42	13	3	6	4	0	
Gout	24	19	17	17	17	6	0	
Rheumatoid arthritis ..	5	7	17	22	30	19	0	
Ankylosing spondylitis	2	4	5	25	45	17	2	
	Normal	Doubtful increase	Increased rate					

CORRECTION FOR ANÆMIA IN RHEUMATISM

The necessity for correction of the B.S.R. for red cell deficiency or excess is disputed. Many workers with wide experience of the test deny that it is necessary. I regard it as desirable for the fullest understanding of the pathological processes at work in the patient, and would decline to give an opinion on a moderately increased uncorrected B.S.R. unless some indication of the presence or absence of anæmia were supplied. Cases are repeatedly seen in which the rate as observed is moderately increased in the presence of anæmia. On correction for packed red cell volume a normal figure is indicated, the clinical inferences of which have been fully supported by the subsequent course of the case. On the other hand, a case of rheumatoid arthritis with marked secondary anæmia will usually show a rapid rate, even after correction for red cell volume deficiency.

At the same time, especially when serial tests are performed, the observed or "crude" rate has much value, being an assessment of the state of the

patient with reference both to anæmia and to the true "B.S.R. factor". In rheumatism this question is complicated by the fact that red cell volume deficiency may be in part the result of hydræmia, as shown by Sparks and Haden (1932) and Robinson (1943). There is some evidence to suggest that this absolute increase of plasma volume may be related to plasma protein changes, consequent on the rheumatic process, but not concerned with the rouleaux-forming effect which is primarily responsible for an increased rate of sedimentation. This question has been discussed by Gibson and Pitt (1946); the suggested hypothesis is shown schematically in table 2.

TABLE 2

Suggested interrelationship of tissue lesions, hydræmia and B.S.R. in rheumatoid arthritis

Tissue lesions

Plasma changes
   Non-rouleaux-forming
   ? Globulins.

Plasma changes
   Rouleaux-forming
     Fibrinogen· + + +
     ? Globulin +

Hydræmia

Large red cell aggregates

Increased B.S.R. +

Increased B.S.R. + + +

For this reason we always record the crude B.S.R. in the form of a curve showing the fall at half-hourly intervals for two hours. On the same chart is recorded the hæmatocrit reading and the corrected rate. This method is especially helpful when repeated tests on the patient are recorded on the same chart. The clinician can see at a glance whether or not the curve has altered. If it has, then the hæmatocrit readings can be compared. If these differ, reference to the corrected rate will show if the variations in the curve can be ascribed to the difference in red cell volume alone. In the Spa Hospitals' method the corrected rate is that which, it is estimated, would have been found if the patient's red cell volume had been 42 per cent. of blood volume. The Wintrobe technique corrects to 47 per cent. in males and 42 per cent. in females.

B.S.R. IN THE CLINICAL TYPES OF CHRONIC RHEUMATISM

Rheumatoid arthritis.—In this condition the B.S.R. is at present the main objective measure of activity or severity of the disease. The rate appears to depend upon the number and size of joints affected and on the intensity of the reaction taking place in them. In terms of morbid anatomy it is probably related to the total mass of fibrinoid necrosis in the patient, to which is

added the effects of lysis of cartilage by synovial pannus and the other destructive lesions in the joints. In the majority of cases the rate is rapid when the arthritic stage has become clinically obvious. In some, the rate may be extreme when the joint signs appear to be slight, perhaps involving only one or two interphalangeal joints. Recent work on the pathology of rheumatoid arthritis has shown that joint lesions are not the only foci of ' activity. Baggenstoss and Rosenberg (1941) found rheumatic heart disease in more than half of twenty-five cases which came to necropsy. In a few of these the same writers (1944) found lesions which they regard as being characteristically rheumatoid in type, differing in structure from the heart lesions of acute rheumatism. Lesions in skeletal muscle have been found by Curtis and Pollard (1940), while Freund *et al.* (1942, 1945) have found perineural and skeletal muscle nodules. It may be that non-articular lesions of this type are responsible for the rapid rates noted, for which the evidence of joint disease appears to be inadequate. A normal rate is infrequent, 5 per cent. in my experience. This may be due in some cases to a tendency for the rate to lag behind the clinical state of the patient. This has been noted at the onset of disease and later when remissions and exacerbations occur. In a very few cases, however, the fact must be accepted that a typical case of active rheumatoid arthritis may have a persistently normal B.S.R., shown over long periods in repeated estimations by all methods. In such cases there appears to be a constitutional inability to elaborate the rouleaux-forming factor; and this emphasizes that the B.S.R., in common with all laboratory tests, is no substitute for clinical judgement.

In the more usual case, however, phases of activity and partial remission are accurately mirrored in the sedimentation rate. The effect of any treatment may be gauged by serial observations of the rate, and only if the disease dies out, leaving purely mechanical deformity, does the B.S.R. return to normal. When gold is used in a favourable case the rate shows a rapid improvement and a return to normal may occur. On the other hand, the rate as shown by the wide-bore tube method with correction for red cell volume frequently stops short of the strict normal. This is a prognostic sign of some importance, because the condition may be expected to relapse. However good the initial response to gold appears to be clinically, prognosis should be guarded unless the B.S.R. attains a strictly normal value and maintains it over a period.

In discussing the remissions associated with jaundice, Gardner *et al.* (1945) noted that the B.S.R. in many cases was lowered before the icteric phase began and that a marked rise in rate occurred after jaundice had cleared. These fluctuations appeared whether or not remission of rheumatic symptoms occurred. They did not correspond to the clinical condition of the joints and appeared to be due to some secondary effect in the liver. These workers concluded that the B.S.R. is not a reliable guide to the arthritic condition during jaundice.

Apart from gold and jaundice, a feature of the B.S.R. in rheumatoid arthritis is its constancy over long periods. Serial curves may be almost identical. This contrasts with gout and subacute rheumatism, in which short term fluctuations are frequent.

Some writers have suggested that the rapid B.S.R. is an indication that rheumatoid arthritis is an infective disease. It is only necessary to point out that increased rates may be found in nephritis, cirrhosis of the liver, pregnancy, certain neoplasms, and gout, to show that this is not a valid argument.

Osteoarthritis.—The sedimentation rate in primary osteoarthritis is never much increased. My experience does not agree with the statement often made that the rate is always normal. In cases of osteoarthritis of the spine or hip in which no evidence exists of infection or gout, it is frequently just above the strict normal. In table 1 it will be seen that the number of cases in the 80 to 89 per cent. group (red cell volume:1 hour) exceeds those in the 90 to 100 per cent. group. The converse holds for fibrositis and the normal control group. It may be stated that a slightly increased or border-line B.S.R. reading does not exclude osteoarthritis. A rate much above normal indicates that if osteoarthritic changes are seen radiologically they are secondary to infection, rheumatoid arthritis or gout, or that the condition may be associated with some non-rheumatic process elsewhere.

Fibrositis.—In this condition the rate is strictly normal and its normality is emphasized by the fact that anæmia is rare. As seen in table 1 the distribution parallels closely the rates in normal control cases. This observation is frequently of great value in the differential diagnosis of the case when first seen. Muscle pain is common in the early and pre-arthritic stages of rheumatoid arthritis. A rapid rate indicates at once that the condition is more than a simple fibrositis. Again, joint swelling, stiffness and pain may be due to periarticular fibrositis. Suspicion of arthritis is aroused, but a strictly normal B.S.R. and hæmatocrit reading are signs that a diagnosis of rheumatoid arthritis with the consequent grave prognosis should not be made at this stage. Slocumb (1940), who has made a special study of periarticular fibrositis, emphasizes the value of a normal B.S.R. in diagnosis.

Sciatica is not associated with a raised B.S.R. if it is due to gluteal fibrositis, a true neuritis of the nerve, or pressure of an intervertebral disc. Severe sciatica with a rapid B.S.R. at once suggests some serious underlying cause, such as pelvic neoplasm.

Gout.—The clinical pattern of gout has been emphasized in the work of Hench (1941), who has described the course as consisting at first of isolated attacks with complete recovery after each. No chronic arthritis is present in this phase. The attacks tend to become more frequent and a residual joint lesion is carried over from one to the other. The final state of the patient may be comparable to that in rheumatoid arthritis in the extent and severity of the joint disorganization.

added the effects of lysis of cartilage by synovial pannus and the other destructive lesions in the joints. In the majority of cases the rate is rapid when the arthritic stage has become clinically obvious. In some, the rate may be extreme when the joint signs appear to be slight, perhaps involving only one or two interphalangeal joints. Recent work on the pathology of rheumatoid arthritis has shown that joint lesions are not the only foci of activity. Baggenstoss and Rosenberg (1941) found rheumatic heart disease in more than half of twenty-five cases which came to necropsy. In a few of these the same writers (1944) found lesions which they regard as being characteristically rheumatoid in type, differing in structure from the heart lesions of acute rheumatism. Lesions in skeletal muscle have been found by Curtis and Pollard (1940), while Freund *et al.* (1942, 1945) have found perineural and skeletal muscle nodules. It may be that non-articular lesions of this type are responsible for the rapid rates noted, for which the evidence of joint disease appears to be inadequate. A normal rate is infrequent, 5 per cent. in my experience. This may be due in some cases to a tendency for the rate to lag behind the clinical state of the patient. This has been noted at the onset of disease and later when remissions and exacerbations occur. In a very few cases, however, the fact must be accepted that a typical case of active rheumatoid arthritis may have a persistently normal B.S.R., shown over long periods in repeated estimations by all methods. In such cases there appears to be a constitutional inability to elaborate the rouleaux-forming factor; and this emphasizes that the B.S.R., in common with all laboratory tests, is no substitute for clinical judgement.

In the more usual case, however, phases of activity and partial remission are accurately mirrored in the sedimentation rate. The effect of any treatment may be gauged by serial observations of the rate, and only if the disease dies out, leaving purely mechanical deformity, does the B.S.R. return to normal. When gold is used in a favourable case the rate shows a rapid improvement and a return to normal may occur. On the other hand, the rate as shown by the wide-bore tube method with correction for red cell volume frequently stops short of the strict normal. This is a prognostic sign of some importance, because the condition may be expected to relapse. However good the initial response to gold appears to be clinically, prognosis should be guarded unless the B.S.R. attains a strictly normal value and maintains it over a period.

In discussing the remissions associated with jaundice, Gardner *et al.* (1945) noted that the B.S.R. in many cases was lowered before the icteric phase began and that a marked rise in rate occurred after jaundice had cleared. These fluctuations appeared whether or not remission of rheumatic symptoms occurred. They did not correspond to the clinical condition of the joints and appeared to be due to some secondary effect in the liver. These workers concluded that the B.S.R. is not a reliable guide to the arthritic condition during jaundice.

The B.S.R. is normal in static or traumatic cases of back pain, in fibrositis of the back muscles, and normal, or nearly so, in osteoarthritis of the spine (spondylitis deformans). It will therefore be seen that the test is of great value in the differential diagnosis of cases with symptoms referable to the spine.

CONCLUSIONS

To sum up, the estimation of the B.S.R. is an almost indispensable step in the management of chronic rheumatic diseases. It separates them into two fairly clear-cut groups:—

(1) Fibrositis and osteoarthritis, in which the rate is normal or nearly so.

(2) Rheumatoid arthritis and ankylosing spondylitis, in which the rate is rapid except in very exceptional cases.

Gout with a fluctuating rate occupies an intermediate position and has the uric acid phenomena to guide the clinician to the diagnosis.

As a test of progress in the second group the B.S.R. provides a yardstick free from any bias on the part either of the patient or of the physician. No claim to cure these diseases can be accepted which is not supported by the unequivocal evidence of this test.

In all forms of chronic rheumatism the necessity for the repetition of B.S.R. estimations is emphasized.

Bibliography

Baggenstoss, A. H., and Rosenberg, E. F. (1941): *Arch. int. Med.*, **67**, 241.
——, —— (1944): *Arch. Path.*, **37**, 54.
Collins, D. H., Gibson, H. J., Race, J., and Salt, H. B. (1939): *Ann. rheum. Dis.*, **1**, 333.
Curtis, A. C., and Pollard, H. M. (1940): *Ann. int. Med.*, **13**, 2265.
Fahræus, F. (1921): *Acta med. Scand.*, **55**, 3.
Freund, H. A., et al. (1942): *Amer. J. Path.*, **18**, 865.
—— (1945): *Science*, **101**, 202.
Gardner, F., Stewart, A., and MacCallum, F. O. (1945): *Brit. med. J.*, ii, 677.
Gibson, H. J., and Kersley, G. D. (1938): *Med. Pr.*, **196**, 353.
—— and Pitt, R. M. (1946): *Ann. rheum. Dis.* (in the press).
Haden, R. L., and Kinnell, J. (1942): *J. lab. clin. Med.*, **27**, 725.
Harkness, J., Houston, J., and Whittington, R. B. (1946): *Brit. med. J.*, i, 268.
Hench, P. S. (1941): *J. Amer. med. Ass.*, **116**, 453.
Kahlmeter, G. (1926): *Acta med. Scand.*, **16**, 352.
McIntosh, D. G., and Keay, D. M. (1945): *Brit. med. J.*, ii, 584.
Pemberton, R. (1935): "Arthritis and Rheumatoid Conditions", 2nd edition, London, p. 117.
Rawls, W. B., Weiss, S., and Collins, V. L. (1937): *Ann. int. Med.*, **10**, 1021.
Robinson, G. L. (1943): *Ann. rheum. Dis.*, **3**, 207.
Rodgers, B. (1945): *Brit. med. J.*, ii, 940.
Shackle, J. (1938): *Brit. J. Rheum.*, **1**, 75.
Slocumb, C. H. (1940): *Ann. rheum. Dis.*, **2**, 108.
Smyth, C. J., Freyberg, R. H., and Lampe, P. (1941): *J. Amer. med. Ass.*, **117**, 826.
Sparks, M. I., and Haden, R. L. (1932): *Amer. J. med. Sci.*, **184**, 753.
Tinney, W. S. et al. (1945): *Proc. Mayo Clin.*, **20**, 49.

The B.S.R. findings follow closely on this pattern. Acute attacks are characterized by a very rapid B.S.R. As the patients are often of plethoric type with high red cell counts and hæmatocrit readings this increase of rate may be masked, especially if the rate is estimated in a narrow tube. The observed rate, even in a very wide-bore tube, may appear normal or nearly so. Only after correction for a hæmatocrit reading, which may be as high as 55 per cent., will the true increase in rate be discerned. There appears to be a definite association between the "full-blooded" state and gout. Tinney *et al.* (1945), who described eight cases in which gout was associated with polycythæmia vera, ascribed it to the nuclear material set free by the excess of maturing normoblasts. The rate rapidly falls on cessation of the gouty attack and it is only in the final stage of chronic active arthritis that the B.S.R. remains high.

It may be noted that the B.S.R. does not parallel the blood uric acid increase. Haden and Kinnell (1942) confirmed the findings of Gibson and Kersley (1938) on this point. The factor of tissue destruction, indicated by the B.S.R., appears to be to a considerable degree independent of the metabolic error.

There is undoubtedly a group of cases of fibrositis in which the blood uric acid is increased but which lack many of the other classical features of gout, including tophi. With some justification the name "gouty fibrositis" has been applied to them. They differ from simple fibrositis in that many cases show an increase in B.S.R. This is not, however, invariable, and the B.S.R. is only important in diagnosis if it is increased and if it is associated with a high blood uric acid.

As would be expected, any heterogeneous group of cases at varying stages of the disease would show widely varying sedimentation rates, as is shown in table 1.

Ankylosing spondylitis.—In general the B.S.R. in this condition is rapid from the earliest clinical stage. Even when radiological evidence of disease is confined to the sacro-iliac joints the rate is increased, and when the arthritic state is fully developed in the vertebral joints the rate is even more rapid than in rheumatoid arthritis. This may be correlated with the rapid advance of the disease, probably as a result of the absence of physiological rest in the costo-vertebral and other joints involved. The "crude" B.S.R. is especially rapid because of the presence of anæmia. Gibson and Kersley (1938) reported the mean packed red cell volume in 64 male spondylitics to be 38 per cent., as compared with the normal 47 per cent. Even on correction, however, the rate remains rapid while the disease runs its relatively rapid course. The only therapeutic measure which influences the B.S.R. is X-ray therapy. Smyth *et al.* (1941) reported an improved B.S.R. in 41 per cent. of 52 cases treated in this way. It may be noted that immediately following X-ray therapy the rate may increase, to be followed by improvement later.

a stormier course than those in whom there is rapid return to their former level after the peak day.

ESTIMATION OF ABNORMAL FINDINGS

It has been stated that if the test is to be of service it must be done regularly, and in conjunction with other tests and X-rays. The rule at King Edward VII Sanatorium is to do a sedimentation test on admission, once per month during the patient's stay, and just before leaving. Should the case at any time, however, show clinical signs of abnormality the test is repeated and if a rise has occurred, and no extrapulmonary cause can be found to account for it, it usually shows that some spread of the disease has taken place.

In *pneumothorax cases* which have a fairly normal rate, a rise often suggests fluid formation: quite often the rise in sedimentation rate will precede the fluid by many days, or even weeks in rare cases. In those cases which develop fluid and return a normal sedimentation rate, it can usually be stated that the fluid will run a benign course and be no trouble in the treatment of the case. If, however, a case of pneumothorax which develops fluid has a very high reading, which remains so, the outlook is not good, and it generally means the fluid will become T.B. positive and eventually turn to pus. The above statement cannot be proved in 100 per cent of cases, and so once again it must be stressed that the test should be used in conjunction with all other clinical data.

In the case of women, the proximity of onset or cessation of *menstruation* has no apparent permanent effect on the sedimentation test. However, menstruation may act as a "booster" (that is, have an aggravating action) on conditions which, in themselves, tend to cause an increase in the sedimentation rate.

It is generally thought that patients who finish their treatment at a sanatorium with a low sedimentation rate, have a better prognosis than those who finish with an increased rate. It would be a foolish physician who would pronounce a case arrested in the face of a rising sedimentation rate, unless there was an obvious extraneous cause for this. It requires the acme of clinical and radiological experience to be able to say in any case that the disease has been arrested and healing begun. A record of decreasing sedimentation rate readings would be a most comforting endorsement in such cases; true, in many it would be unnecessary.

CONCLUSION

The sedimentation rate, if properly used, can be of great value in the treatment and prognosis of pulmonary tuberculosis, but done as an isolated test, or read with the wrong meaning, it can do nothing but harm.

If a series of sedimentation tests in a given patient are all low except one, this can be neglected in the prognosis, provided low readings follow and continue until the end of treatment.

THE BLOOD SEDIMENTATION RATE IN PULMONARY TUBERCULOSIS

By G. S. TODD, O.B.E., M.B., Ch.M., F.R.C.P.

Medical Superintendent, King Edward VII Sanatorium, Midhurst.

VARIOUS methods of performing the blood sedimentation test are used in England, of which the best known is the Westergren method. The method in use at King Edward VII Sanatorium, Midhurst, is the micro-method, in which the tube is graduated in millimetres to 100. This is simple to perform, not necessitating venous puncture, and gives satisfactory results. It was found, some years ago, that on cold days certain cases gave false readings. After prolonged trials the discovery was made that putting the graduated tubes in a water bath at 37° C., and reading them at the end of half an hour, gave similar readings in the majority of cases to one-hour readings at room temperature.

PROGNOSTIC AND CLINICAL SIGNIFICANCE

The value of blood sedimentation in pulmonary tuberculosis is high, provided it is assessed in the right manner. A patient who has a normal sedimentation rate on admission, and remains normal throughout the treatment, can be considered to have a good prognosis. It is generally found in these patients that the intrapulmonary lesion is small and that, in the majority of cases, there are no physical signs in the chest.

In normal cases of *uncomplicated pulmonary tuberculosis* the sedimentation rate follows (literally follows, as it is usually several days behind) fairly faithfully the condition of the patient as observed clinically, provided a correct interpretation be given to it. It is generally believed that the magnitude of a given rate represents the product of the amount of tissue involved, and the rapidity with which that involvement is taking place. One great exception to the rule, however, is *pleural effusion*. At the onset of a pleural effusion the sedimentation rate is often exceedingly high, and yet breaking down of tissue is not taking place to any extent. However, the readings in cases of primary pleural effusion rapidly return to normal, unless complications occur, such as a spread of the disease to the lung, or the invasion of the fluid by secondary organisms : these patients will continue to have a high sedimentation rate for several months.

Reaction after thoracoplasty.—An interesting fact about the sedimentation rate is the way patients undergoing thoracoplasty react. For instance, a patient may have a blood sedimentation rate in the region of 10 per cent. If the test is done daily after the operation, in a number of cases it will be observed that the peak rate is usually reached on the fourth day after the first stage of the operation, and on the third day after the second stage. It then begins to return to its former level. Should the test run very high for some time, after the fourth day, it is an indication that the patient will have

THE TEST IN ACUTE RHEUMATISM

In acute rheumatic fever the B.S.R. will of course be raised, and in the presence of fever, acute arthritis and at the onset of carditis the test is really superfluous. Its great value arises later when the temperature and pulse rate have subsided and the joints are no longer inflamed. At this stage a heart lesion may be present and the practitioner in charge of the case has to decide when it is safe to allow the patient out of bed. It is now generally accepted that, with one or two exceptions to be mentioned later, a normal B.S.R. is a reliable indication that the rheumatic process is no longer active and that rest can be relaxed. Generally, the onset of acute rheumatism produces a steep rise or increase in the B.S.R., whilst the fall to normal is a gradual process, taking several weeks or even months, especially when the heart has become involved. Sometimes the rheumatic process overwhelms the patient's defences to such an extent that it continues unabated or with only slight remissions until cardiac failure appears and ultimately proves fatal. Cases are on record in which this smouldering infection can continue for quite two years and the B.S.R. never become normal. Fortunately this is not the usual course of events, but with the familiar tendency of rheumatism to relapse, a child who has recently suffered from an acute attack should be re-examined at regular intervals and have the B.S.R. checked for any signs of recurrence.

CHOREA

It has become clear that correlation between the speed of the B.S.R. and the degree of active disease present, noted in various forms of acute rheumatism, does not hold good in regard to chorea. In fact, the most severe cases of chorea are often associated with an abnormally slow rate; so much so that it has been questioned whether B.S.R. values in the upper limits, generally regarded as normal, should be considered in chorea as a sign of active disease. On the whole, chorea generally produces a slight alteration in the B.S.R., but the test does not permit the selection of patients who are likely to develop cardiac disease.

SUBACUTE RHEUMATISM

There is certainly a tendency to make a diagnosis of subacute rheumatism too frequently. It has long been realized that growth is a painless process, but there are causes other than rheumatism that produce the odd ache, particularly when it is confined to the legs. Faulty posture is often the basis of the complaint. The B.S.R. is of considerable help in sorting out these cases and with a normal figure active subacute rheumatism can be excluded. On the other hand, in old rheumatic cases a temporary increase in the B.S.R. has been repeatedly observed with the return of pains in the limbs. Generally

THE BLOOD SEDIMENTATION RATE IN RHEUMATIC FEVER

By BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.

Physician, Hospital for Sick Children, Great Ormond Street, and Royal Northern Hospital.

PHYSICIANS of the present generation may still be able to recall the emphasis laid by some of their teachers upon the importance of nursing all children with rheumatic fever strictly recumbent for an arbitrary period of three to six months. Fortunately, knowledge of the rheumatic process has advanced to a degree that such children are now no longer condemned to months of inactivity in bed, irrespective of whether or not their rheumatic state is active or, in fact, whether their heart is affected at all. Conversely, a smouldering rheumatic lesion is not so likely to escape detection, and at this critical stage appropriate steps can be taken to give it the maximum of rest.

Although the actual cause of rheumatism still remains unsettled, the pathogenesis of the disease has become much clearer. Not only is it now possible to exclude a few disorders in childhood that might be mistaken for rheumatism, but clear diagnostic criteria have been established which differentiate with some certainty a quiescent from an active rheumatic state. Fever, tachycardia, failure to gain weight, an obviously progressive cardiac lesion and the presence of a circinate rash or nodules are all familiar signs of active rheumatism. Such evidence is not infallible: acute carditis may be afebrile, and tachycardia and a stationary weight chart may have other causes. An additional and more delicate test is required.

The observations of Fahræus on the rapidity of sedimentation of erythrocytes in different diseases led two other Scandinavian physicians, Westergren and Kahlmeter, to apply the method to rheumatism twenty years ago, and the test is now universally accepted in the clinical investigation of the disease. In this country, it has been in use for the last fourteen years (Bach and Gray Hill, 1932; Payne, 1932; Payne and Schlesinger, 1935; Brown and Weintraub, 1941).

With children, one of the micro-methods is the best. A prick in the pulp of the finger is much more familiar and less terrifying than the paraphernalia of a needle, a syringe and venepuncture. Only 0.4 c.cm. of blood is required; the necessary technique is easily acquired and, with practice, can be applied at the bedside with the minimum of apparatus.

Before interpreting the result of a blood sedimentation rate (B.S.R.), the clinician must be quite clear what to expect from the test. He must realize that it is non-specific and that a rapid B.S.R. may be associated with any bacterial infection and with most fevers. Such intercurrent infection must therefore always be excluded when carrying out the test in rheumatism.

continue in this manner for months, the number of nodules varying from time to time, and the prognosis is left in doubt. Many ultimately recover, but others suddenly deteriorate and, overwhelmed by a gradual increase in their rheumatic lesions, finally succumb (see fig. 1 and 2).
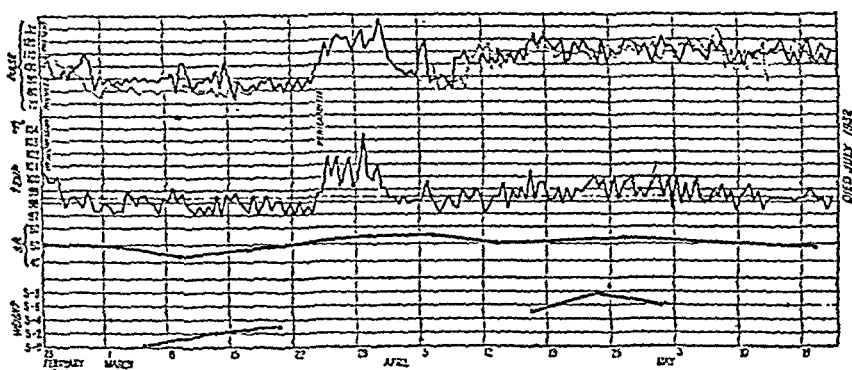

FIG. 2.—Persistently raised B.S.R. in the presence of nodules, active disease still present: terminated in death.

MINIATURE RHEUMATIC FEVER

The test is a useful guide in rheumatic subjects who have recently suffered from an attack of acute tonsillitis, which is notoriously apt to produce a rheumatic relapse. Every degree of relapse can occur, varying from an acute and virulent pericarditis with early death to the mildest rheumatic incident, best termed "miniature rheumatic fever". This last form is characterized by slight degrees of fever, transient tachycardia and a persistent or fresh rise in the B.S.R. after the tonsillitis has subsided. The mildest cases show no changes in the temperature or pulse chart and only the B.S.R. is affected; apart from this they would easily pass unnoticed. These events demonstrate the latent tendency of rheumatic patients to relapse after an acute hæmolytic streptococcal throat infection (see fig. 3).

FALLACIES IN THE B.S.R. TEST

Certain effects of a non-rheumatic nature must be taken into account. Polycythæmia, liver disease or damage, with a consequent decrease in the plasma fibrinogen, and allergic states, all tend to decrease the B.S.R. But the most important fallacy in connexion with acute rheumatism is the slow rate which may occur in the later stages of *congestive cardiac failure*. However active the rheumatic process may be, the onset of failure and œdema causes the B.S.R. to decrease. Previous rapid rates are replaced by a figure which in other circumstances would be considered normal. Tendency to revert to a normal B.S.R. may occur before any gross signs of failure are

the temperature is hardly affected and the whole episode is over in a few days. There may already be heart disease present in these subacute rheumatic cases, dating from a previous attack, and the question then arises whether or not there is any fresh cardiac involvement. In the absence of any clinical evidence the B.S.R. furnishes the best answer, and if it is normal there is no indication for drastic precautions.

SYSTOLIC MURMURS AND THE B.S.R.

The discovery of an apical systolic murmur in a child always raises diagnostic problems and a decision must be reached whether this is the result of an early carditis or merely associated with posture, anæmia or a minor congenital malformation. This differentiation is particularly difficult in the absence of cardiac enlargement or when there has been a recent history of throat infection, arthritis or chorea. Help can again be obtained from the B.S.R., and if it is normal the murmur can usually be dismissed as of little consequence.

NODULES

The presence of nodules indicates a widespread infection which is likely to prove serious, but there is generally an appreciable lag in the time they appear and disappear in relation to other rheumatic manifestations. It may therefore be difficult to decide what stage the disease has reached in a particular case. Here the B.S.R. may have considerable prognostic value, since the first indication that nodules are about to vanish is a gradual return of an increased B.S.R. to normal. Conversely, a persistently raised B.S.R. is clear evidence that the end of the active phase has not been reached and that nodules are likely to remain for an indefinite period. Such patients may
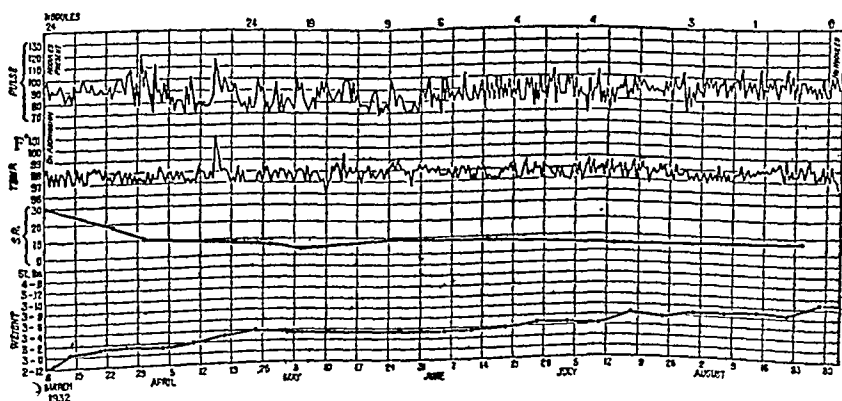
FIG. 1.—To show falling B.S.R. in the presence of nodules, active phase over, nodules disappear later.

THE EFFECT OF OTHER INFECTIONS

Acute tonsillitis generally produces an increase in the B.S.R. lasting for two or three weeks, after which it drops to normal. A relapse or some other complication, such as otitis or adenitis, will delay this. In comparison with active rheumatism these upper respiratory infections cause only a temporary rise (Brown and Weintraub, 1941). Some authors (Bachal and Struthers, 1939) believe that such incidents produce a more marked or prolonged alteration in rheumatic subjects, but, as previously mentioned, the question of a fresh wave of acute rheumatism always arises.
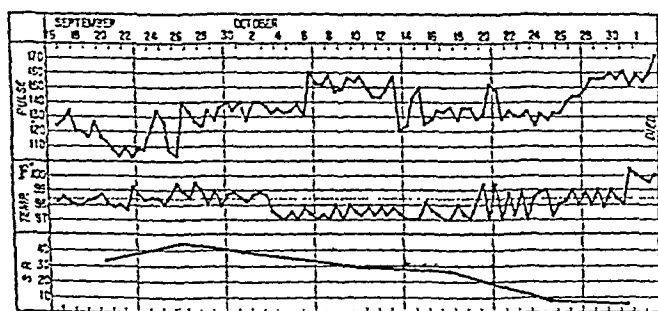
FIG. 4.—Cardiac disease. To show the fall of the S.R. with onset of congestive cardiac failure.

Influenza seems to have a particularly disturbing effect on the B.S.R., whereas the *common cold* and *chronic tonsillar sepsis* produce little and certainly no constant alteration.

Rheumatoid arthritis, in its earliest stages, may cause confusion. No arthritic changes may have arisen and, apart from fleeting joint pains, tachycardia and stationary weight, a considerable increase in the B.S.R. without apparent cause is the only prominent feature. Tuberculosis and congenital syphilis have also sometimes to be excluded.

METHOD EMPLOYED

Many ways of estimating the B.S.R. have been devised and each has its advocates. The results obtained from a macro-method compare very closely with those produced by a micro-method, although the former, having a higher range, is said to be the more sensitive (McKinley and Jackson, 1944). As a practical proposition a micro-method requiring the simplest technique is preferable in dealing with juvenile rheumatism.

Eight to 10 mm. in one hour can be taken as the average normal, although slightly higher figures are occasionally obtained in health (Herzog, 1941). Little reliance should be placed on a single test. Estimations repeated at fortnightly intervals give much more definite information.

noticed, and undoubtedly it often precedes the appearance of œdema, coinciding rather with the hepatic enlargement. Usually this sequence of events has a bad prognosis but recovery can occur and, as failure is overcome, the B.S.R. rises again to its former rapid level associated with the active rheumatic infection which remains (see fig. 4). *Anæmia* increases the B.S.R.,
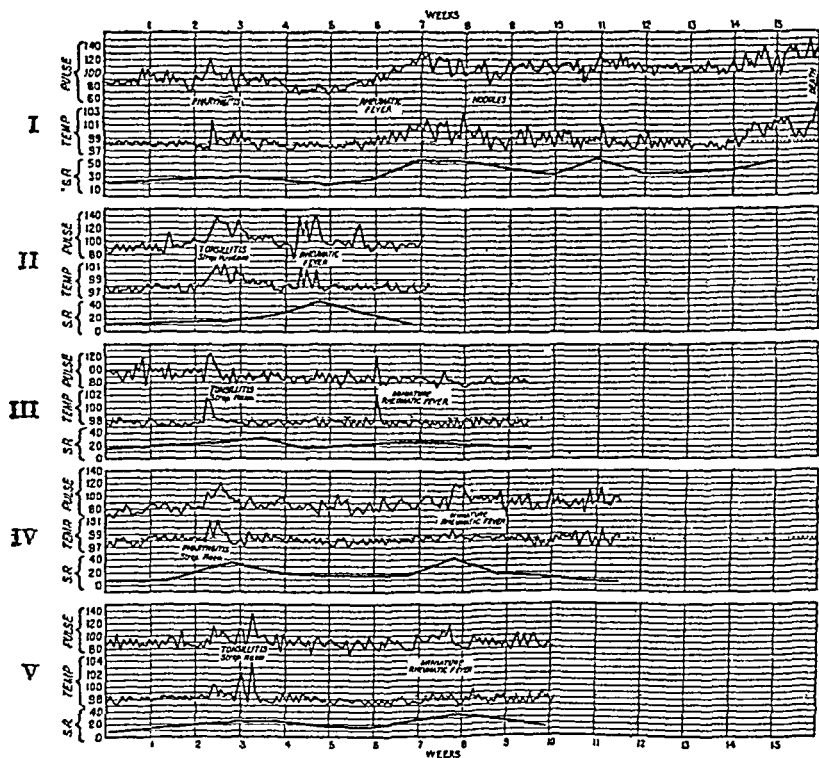

FIG. 3.—To show subsequent course of rheumatic cases following an acute upper respiratory infection.

   (I) Rheumatic fever, pericarditis, nodules with fatal result.
   (II) Rheumatic fever. Rise in pulse, temperature, B.S.R.
  (III) "Miniature rheumatic fever". Transient rise in temperature and pulse. Rise in B.S.R. of longer duration.
  (IV) "Miniature rheumatic fever". Rise in pulse rate, negligible rise of temperature. Definite rise of B.S.R.
   (V) "Miniature rheumatic fever". Slight rise in pulse rate, no rise of temperature. Definite rise of B.S.R.

and severe degrees of this must therefore be taken into account when carrying out the test. The degree of anæmia generally encountered in acute rheumatism is not as a rule sufficient to upset the interpretation of the figure obtained and corrections are not necessary. Katamenia in adults also tends to give false rapid readings, so that obviously it is advisable to choose a free intervening period for B.S.R. estimation.

SEA-SICKNESS

By W. R. TROTTER, D.M., M.R.C.P.

DURING the war a considerable amount of research was undertaken, both in this country and in America, with the object of preventing sea-sickness in troops about to take part in an invasion. The present article seeks to apply the lessons thus learnt to the problem of sea-sickness in civilian passengers. It is worth remarking that the investigations in question could only have been carried out in time of war, for they involved subjecting large numbers of unselected men to violent motion on the sea, in the air or on specially devised machines, in order to test out various methods of prevention. Passengers travelling in the luxury liners of peace time may well spare a grateful thought to the unsung heroes who acted as involuntary guinea-pigs in these experiments. Although no remarkable discovery emerged from these investigations, they did at any rate succeed in establishing a few firm facts in a domain of medicine previously dominated by impression and speculation.

PHYSIOLOGY

Sea-sickness is manifestly caused by the motion of the sea, acting on a susceptible subject. This statement may with some plausibility be analysed a little further.

First, it may be said that alternating acceleration in a vertical plane is probably the operative factor in the sea's motion. There is no evidence that complex types of movement, such as yawing or the "corkscrew" effect so much feared by the nervous passenger, are of any particular significance.

Secondly, it would appear that the tendency of a particular motion to produce sickness is not related in a simple fashion to the degree of vertical acceleration. The periodicity of the alternating acceleration is also important, and there is an optimum degree of acceleration, increase beyond which it is less effective. In practice it is found that vessels of small to medium size (such as M.L.'s and destroyers) have the highest sickness rates. In very small craft, such as rowing-boats, the periodicity of the motion is too rapid to have the maximum effect, whilst in large liners it is too slow. Similarly, in small craft, pitching has a periodicity nearer the optimum than rolling and hence causes more sickness; whereas in large vessels the reverse generally holds good. In general, the violent and irregular accelerations met with in aircraft are less incapacitating than the more subdued and regular motion of a ship.

The way in which motion of the effective type operates on the human body to produce sickness is not yet fully understood. The balance of evidence supports the view that the receptor organ is the vestibular apparatus of the inner ear. It is likely that the utricle, rather than the semi-

✓   COMPARISON WITH OTHER BLOOD TESTS

During the last few years one or two further blood tests have been employed in acute rheumatism. In America the *Weltmann reaction* has had a particular vogue. It is thought that this test and the B.S.R. depend upon changes in the alpha-globulin and plasma fibrinogen, and the behaviour of both tests follow each other closely according to the stage of the disease. The Weltmann reaction is considered by some to be more delicate, as it is abnormal more often than the B.S.R. in the presence of active rheumatism. It is also said to be more reliable since, compared with the B.S.R., it is less frequently affected when the rheumatic process appears to be quiescent (Shulis and Levy, 1943). Possibly the stage of the disease can be estimated with greater accuracy by the Weltmann reaction (Klein, Levinson and Rosenblum, 1940).

The *formol gel test* seems to have no advantage over the B.S.R. except that its accuracy is not affected by keeping the drawn blood for any length of time and therefore the test need not be so promptly carried out (Butterworth and Poindexter, 1942).

All are agreed that these additional blood tests are valuable only as complements to the B.S.R. and should not supplant it. Requiring a somewhat complicated technique, they are not recommended as practical bedside propositions. The B.S.R. provides all the additional help that the clinician requires.

Thanks are due to the Editors of the *Archives of Diseases of Childhood* for permission to reproduce the charts (fig. 1-4).

References

Bach, F., and Gray Hill, W. (1932): *Lancet*, i, 75.
Bachal, H. L., and Struthers, R. R. (1939): *Canad. med. Ass. J.*, **40**, 140.
Brown, E. E., and Weintraub, C. (1941): *Amer. Heart. J.*, **22**, 342.
Butterworth, J. S., and Poindexter, C. A. (1942): *Amer. J. med. Sci.*, **203**, 278.
Green, C. A., Thomson, S., and Glazebrook, A. J. (1939): *Ann. rheum. Dis.*, **1**, 180.
Herzog, R. S. (1941): *J. lab. clin. Med.*, **27**, 355.
Klein, R. I., Levinson, S. A., and Rosenblum, P. (1940): *Amer. J. Dis. Child.*, **59**, 48.
McKinley, J. B., and Jackson, R. L. (1944): *Ibid.*, **67**, 474.
Payne, W. W. (1932): *Lancet*, i, 74.
——, and Schlesinger, B. (1935): *Arch. Dis. Child.*, **10**, 403.
Shulis, S., and Levy, D. S. (1943): *Amer. Heart J.*, **26**, 355.

SEA-SICKNESS

By W. R. TROTTER, D.M., M.R.C.P.

DURING the war a considerable amount of research was undertaken, both in this country and in America, with the object of preventing sea-sickness in troops about to take part in an invasion. The present article seeks to apply the lessons thus learnt to the problem of sea-sickness in civilian passengers. It is worth remarking that the investigations in question could only have been carried out in time of war, for they involved subjecting large numbers of unselected men to violent motion on the sea, in the air or on specially devised machines, in order to test out various methods of prevention. Passengers travelling in the luxury liners of peace time may well spare a grateful thought to the unsung heroes who acted as involuntary guinea-pigs in these experiments. Although no remarkable discovery emerged from these investigations, they did at any rate succeed in establishing a few firm facts in a domain of medicine previously dominated by impression and speculation.

PHYSIOLOGY

Sea-sickness is manifestly caused by the motion of the sea, acting on a susceptible subject. This statement may with some plausibility be analysed a little further.

First, it may be said that alternating acceleration in a vertical plane is probably the operative factor in the sea's motion. There is no evidence that complex types of movement, such as yawing or the "corkscrew" effect so much feared by the nervous passenger, are of any particular significance.

Secondly, it would appear that the tendency of a particular motion to produce sickness is not related in a simple fashion to the degree of vertical acceleration. The periodicity of the alternating acceleration is also important, and there is an optimum degree of acceleration, increase beyond which it is less effective. In practice it is found that vessels of small to medium size (such as M.L.'s and destroyers) have the highest sickness rates. In very small craft, such as rowing-boats, the periodicity of the motion is too rapid to have the maximum effect, whilst in large liners it is too slow. Similarly, in small craft, pitching has a periodicity nearer the optimum than rolling and hence causes more sickness; whereas in large vessels the reverse generally holds good. In general, the violent and irregular accelerations met with in aircraft are less incapacitating than the more subdued and regular motion of a ship.

The way in which motion of the effective type operates on the human body to produce sickness is not yet fully understood. The balance of evidence supports the view that the receptor organ is the vestibular apparatus of the inner ear. It is likely that the utricle, rather than the semi-

circular canals, actually initiates the impulses, since nystagmus has not been observed in sea-sick persons.

Both experience and experiment have shown that motion sickness is most readily produced when the head is held upright, and least readily when it is horizontal. The sufferer from sea-sickness instinctively, and quite rightly, lies flat on his bunk when the malady comes upon him. It would seem that it is the position of the head that is important; that of the rest of the body is immaterial.

The *symptomatology* of sea-sickness is too well known to need description here. It is, however, worth remarking that the distinction which used to be drawn between "vagotonic" and "sympatheticotonic" persons, who were supposed to react to sea-sickness in different ways, cannot now be regarded as having any practical significance. The distinction was largely based on whether the pulse rate was fast or slow. It is true that sea-sick persons may have either fast or slow pulse rates; but so also may persons subjected to the motion of the sea, but not made sick by it: the bradycardia observed in such persons can sometimes be quite striking.

Individual susceptibility.—In concluding this section it must be noted with regret that there is as yet no answer to the most interesting question connected with this subject: namely, what exactly constitutes the difference between a person who is susceptible to sea-sickness and one who is not? This question was investigated during the war, for it was hoped that a method might be found of eliminating susceptibles from recruits to the Commandos. No such method was found; even when the men to be tested were swung on a large swing until a proportion of them were sick there was still no exact correspondence between those who were sick on the swing and those who were sick on the sea. Similarly, there seems to be no exact relationship between susceptibility to sea- and air-sickness, although it is true in a general way that those who are prone to one type of motion-sickness are more likely to suffer from other forms of motion than the average person. It is said that those susceptible to the motion of small craft are not necessarily affected by the motion of large vessels, and *vice versa*; although it is hard to be sure of the truth of this statement. These considerations may lead to speculation as to whether such differences are not determined by small variations in the structure of the utricle, causing it to respond to different types of motion in different people. Such anatomical variations might indeed explain the difference between susceptibles and non-susceptibles. There is, however, no evidence either for or against these speculations.

PSYCHOLOGY

A severe bout of sea-sickness is undeniably an unpleasant experience. The popular idea of the victim as a figure of fun, and hence a rather despicable object (the by-product of a proud seafaring tradition), does not

make it any easier to bear. Sudden, incapacitating illness is always rather humiliating to a hitherto healthy person. The act of vomiting itself induces disgust; whilst to women the devastating effect of intense vasoconstriction on the complexion is an added source of shame. Even to the psychologically stable, sea-sickness brings mental as well as physical discomfort.

For these reasons, an attack of sea-sickness is apt to leave behind it a pungent mental aroma, which is prone to re-assert itself each time the subject embarks. This tends to predispose him to a further attack. In neurotic subjects this tendency is still more marked; whilst to the hypochondriac a sea voyage provides an opportunity of demonstrating an exquisite sensibility to the slightest motion and hence of exciting sympathy. In such people the symptoms of sea-sickness can occur in a completely calm sea; an example is the lady who was placidly enjoying her dinner until told that the ship was entering the Bay of Biscay, whereupon she clapped her hand to her mouth and fled from the saloon in disorder.

Such extreme instances are not, I think, common. In the popular mind the importance of psychological factors in the causation of sea-sickness is exaggerated rather than underestimated. The hearty gentleman in the bar who loudly proclaims that "sea-sickness is purely psychological" is not merely being tactless; he is also talking through his hat. Sea-sickness has a physical basis, but like other physical maladies it can be made much worse by mental factors; just as convalescence from a fractured femur can be delayed by the patient's attitude towards his condition. The importance of the mental factor in sea-sickness must always be remembered; but nothing can have a more disastrous effect on a genuine sufferer than to assure him that his malady is purely imaginary.

PREVENTION

No infallible method of preventing sea-sickness is at present known. The practitioner called upon to advise a potential sufferer must rely upon a combination of general recommendations and the administration of suitable drugs. As a rough estimate it may be said that between half and three-quarters of susceptible persons can be protected against sea-sickness, whilst most of the remainder should obtain some amelioration of their symptoms.

Assurance.—Every effort should be made to change the attitude of fatalism or sheer panic so common among those who have suffered in the past into something more rational. It should be explained that sea-sickness may occur to anyone (the example of Nelson is useful in this connexion), that it does not involve any disgrace, and that attempts to "fight it by will-power" merely make matters worse by concentrating the attention on an event which may never happen. It is worth pointing out that rough seas are on the whole a rarity; any investigator who has had to spend weary days or weeks waiting for weather suitable for sea-sickness trials will

endorse this with feeling. In most long voyages the motion of the ship increases by gradual degrees, thus enabling adaptation to take place. Adaptation is a fairly rapid process in most people, who usually acquire a considerable amount of immunity in a few days; although a few unfortunates never do so. On the whole the facts of the situation are a lot more favourable than the potential sufferer supposes, so that the practitioner is amply justified in taking an optimistic attitude.

It will be seen that there is nothing to gain but much to lose by adopting elaborate precautions before rough weather is actually encountered. To prescribe a special diet, sedatives, purgatives or other drugs while the ship is proceeding placidly on her way through a calm sea is to invite the subject to anticipate future unpleasantness.

Once the motion of the ship has become such that sickness is likely to occur, the time has come to administer an anti-sea-sickness drug. It should be remembered that once nausea has begun the absorption of any drug given by mouth becomes slow and uncertain. It has been shown in experimental motion-sickness that with the onset of nausea the stomach becomes dilated and inert, and normal peristalsis ceases. Hence drugs given at this stage will not be absorbed when wanted, and there is a possibility that several doses will accumulate in the stomach and be absorbed simultaneously when normal tone returns. Administration should therefore begin, if possible, before the onset of nausea.

Drugs.—Of the known preventative drugs *hyoscine* appears to be the most effective and there would seem to be no good reason for employing any other. As there is no evidence of any synergistic action between hyoscine and other drugs there is no justification for the various combinations used by commercial firms; except that sedatives such as phenobarbitone may usefully be added when dealing with nervous subjects, or else given separately at night. For short trips, it has been shown experimentally (Holling, McArdle and Trotter, 1944) that hyoscine in a dose of 0.6 mgm. (1/100 grain) protects about half, and in a dose of 1.2 mgm. (1/50 grain) nearly three-quarters, of susceptible subjects. In the experiments referred to, the drug was given about an hour before encountering rough weather, and its effect lasted for from four to six hours. It was well tolerated (the subjects were, of course, fit young men) and exhaustive tests showed no loss of efficiency. The only symptom noted was dryness of the mouth, often sufficiently marked to make mastication difficult. It may be remarked that the dangers of oral hyoscine are probably overestimated by the profession, perhaps as the result of Dr. Crippen's bold experiment. A single dose of 0.6 mgm. can safely be recommended for any adult for a short trip, such as a Channel crossing; a healthy young adult, of average build, who is particularly susceptible should be advised to take 1.2 mgm. (1/50 grain). The usual preparation of hyoscine is the hydrobromide, made up in tablets, each containing 0.3 mgm. (1/200 grain).

On long voyages, the most generally applicable plan is to prescribe 2 tablets [0.6 mgm. (1/100 grain)] to be taken one hour before rising in the morning, followed by 1 tablet [0.3 mgm. (1/200 grain)] one hour before lunch, and 1 tablet one hour before the evening meal. The total daily dose is 1.2 mgm., and this can be given to any adult for several days on end. With a patient under my personal supervision I should not hesitate to exceed this dose if it seemed necessary. Dryness of the mouth is to be expected and indicates that the drug is being satisfactorily absorbed. The spacing of the doses is designed to ensure that the subject is under the influence of the drug at meal times. The larger dose in the morning is needed to build up the tissue concentration, which presumably falls during the night.

General measures.—The type of food recommended is not of much importance. A nauseated person will in any case avoid fatty food. Perhaps the most important point is to encourage the subject to eat, even though he be reluctant to do so. The presence of food tends to stimulate the atonic stomach and consequently to diminish nausea. It is probably an advantage to restrict fluids, but this advice may be hard to follow if much hyoscine is being taken, for the lack of saliva makes it difficult to swallow dry food. In established sea-sickness, sailors recommend a diet of dry biscuits or dry bread, to be nibbled in small quantities at frequent intervals; this is probably sound advice.

Apart from drugs, numerous other devices have been advocated for the prevention of sea-sickness (such as, for example, a belladonna plaster or a tight binder applied to the abdomen), but I know of no evidence that they are effective. The desirability of directing the gaze at the horizon or at some point on the ship is often discussed; I have not been impressed by the importance of visual factors, although there is some evidence that the sickness rate in aircraft is increased when the view outside is restricted.

TREATMENT

Treatment is on the same lines as prophylaxis; it is in fact prophylaxis carried out too late, and is correspondingly less effective. The object is to ameliorate the symptoms enough to permit of hyoscine being absorbed by mouth. This can usually be achieved by the rigid assumption of the supine position, with the head quite flat, for some hours. Once hyoscine has been absorbed the regime for prevention can be followed. If vomiting or extreme nausea prohibits the absorption of the drug it would seem reasonable to try an injection of 0.3 to 0.6 mgm. (1/200 to 1/100 grain); I have no personal experience of this measure but should not hesitate to use it if it seemed to be indicated.

Reference

Holling, H. E., McArdle, B., and Trotter, W. R. (1944): *Lancet*, i, 127.

ICE AND ICE CREAM

By C. G. LEAROYD, M.R.C.S., L.R.C.P.

MAN seems to have an instinctive suspicion that anything that is very pleasant is bad for him and this must have been of great value in keeping him from excesses. It is the origin of all flesh-mortifying and was probably at the bottom of that little trouble in the Garden of Eden. It is, however, blind; fiction, fruit, and freedom from stifling clothing have all had to be reasoned for in remembered times in face of its unthinking frown.

THE CALORIE VALUE OF ICE CREAM

Ice cream and ices are in this country now in the state of being freed from the stigma of mere pleasantness. They are confections and luxuries and children love them, so probably they ruin the digestion, sap the moral fibre and are dietetically contemptible. This at any rate is not true of a properly constituted ice cream, which has no legal definition, but which the Ice-cream Association of Great Britain and Ireland define as "a frozen product containing not less than 8 per cent. milk fat and not less than 10 per cent. solids-not-fat" or "not less than 8 per cent. butter-fat and 18 per cent. total milk solids", so that in fact it contains the virtues of milk in concentrated form.

Of course, much of what is sold as ice cream falls short of this standard, especially now in these hungry forties; iced custard, iced cornflour with a dash of vanilla would be more accurate descriptions. But real ice cream is an ideal food of particular value in the dietary of the sick and the under-nourished, and is almost all-sufficing. Rats fed for three months on ice cream alone attained normal or nearly normal weight and size, and although they did not do quite as well as their litter mates whose diet included only one-third by weight of ice cream, they did very much better than those on a basal diet. A similar experiment on man would entail his eating about three quarters of a gallon of ice cream a day to get his 3,400 calories and does not seem to have been attempted, although no doubt it would be easy to get young volunteers.

But it is across the Atlantic that people have gone furthest in freeing themselves from the inhibition against this form of food, although they cannot claim to have originated it, as ices were being served at a banquet given by Charles I. Here are a few statistics from the U.S.A. where ice cream making is a great industry; in 1942 the population ate 2,115 million pounds of it and got two million million calories out of it; in 1943 the consumption was three gallons a head and the cost was 1,236,432,000 dollars, a quarter the value of the whole milk and over twice the retail value of the eggs, apples or potatoes consumed annually; the product of a million cows goes into the manufacture of ice cream each year, also 71,000,000 pounds of fruit and 7,000,000 pounds

of nuts; a big factory will turn out 20,000 gallons a day. So with the Americans it is an important article of diet and they are getting over the stage of looking upon it as a mere luxury. It is habitually eaten throughout the year in health and in sickness, so it is well worth while knowing something about its manufacture. Let us look at an ideal laboratory where ice cream makers are taught, and trace it through its five stages.

THE PROCESS OF MANUFACTURE

(1) *Making and pasteurization.*—To make one hundred pounds of ice cream take 24.4 pounds of cream (40 per cent.), fifty-six pounds of whole milk, fifteen pounds of cane sugar, four pounds of skimmed milk powder and 0.3 of a pound of gelatin. The ingredients are mixed and pasteurized at 145° for thirty minutes. The New York State stipulates that the mix shall be pasteurized at 150° for thirty minutes and our own Ministry of Food requires every manufacturer of ice cream in which dried eggs are incorporated to obtain a licence and to agree to subject the mix to 165° for thirty minutes, but this is meant to protect chiefly against the Salmonella gang which are known to occur in dried eggs. The reason why pasteurization rather than sterilization is employed is that overheating or heating for too long gives a cooked flavour to the product, robbing it of its pristine charm. The small maker often avoids pasteurization, milk and some made-up ice cream powder being mixed and frozen, the so-called "cold mix".

(2) *Homogenization.*—It is desirable that this should be carried out at pasteurization temperature. In an ideal plant this is done at 2,500 pounds pressure per square inch, but in the back-room manufacture where the mix may be made in the household copper it is omitted. The commercial point of it is that it ensures a better product and makes pasteurization more efficient by splitting up the fat globules, but from the medical point of view it also gives a much greater digestibility, and homogenized ice cream has been successfully used in the treatment of marasmic infants, in one reported case as young as three months.

(3) *Cooling.*—Speedy temperature reduction is essential in order to stop bacterial growth, which is most probable between 110°-70°. In the Ministry of Food's regulation, already referred to, the mix must not be kept at atmospheric temperature for more than an hour before pasteurization and must be cooled down to 40° within half an hour after it. The high bacterial count in the cottage type of ice cream is generally due to slow cooling, and so were three outbreaks of staphylococcal poisoning, two in Oxford City and one in an American hospital nearby, a sad little story centring around Private G., of the U.S.A. Army.

In order to satisfy their compatriots' craving for the national dish the kitchen staff of a U.S.A. Army unit made a mix of sugar, cornflour and water, boiled it, added powdered milk, dried eggs and vanilla, allowed this to stand in the warm kitchen over-night, and then sent it away for freezing. Some of it found its way into civilian stomachs, with the result that their Oxford owners in two to three hours

suffered from vomiting, abdominal pain, diarrhœa and collapse. The second out-break occurred in five hundred patients and staff of an American hospital. Both outbreaks were tracked down to an enterotoxin from a *Staphylococcus aureus* (type 42D) inhabiting Private G., who helped in the making. The third outbreak was also caused by ice cream prepared by the U.S.A. Army which somehow found its way to civilians in Oxford City, but as the culprit here was also a coagulase-positive staphylococcus, but of type 17, Private G. was probably not concerned. One can, however, was sent to the laboratory of a hospital for examination, but was eaten by the pathologist and sixteen others, who all suffered. Whether this was due to a mistake or whether they were martyrs to greed or science is not stated—a tantalizing omission.

While we are waiting for our mix to cool we may briefly consider *the bacteriology* of ice cream, which is chiefly that of milk. Considering the large amount of ice cream eaten, illness coming from it does not appear to have been on a big scale. There have been some outbreaks of typhoid, a notable one being at South Shields, two hundred cases in 1916; of paratyphoid in the Eastern counties, Wisbech thirty in 1923 and Norwich sixty in 1926; but it may be noted there were some large outbreaks in Birmingham, Bristol and Liverpool, coming from the more dangerous synthetic cream, in 1941; one outbreak of dysentery in Worcester, twenty-four cases and one death; one of diphtheria in Glasgow in 1937, thirteen cases and six deaths, traced to a nasal-carrying maker; and a number of streptococcal sore throats and scarlet fever, of which there have been some sizeable outbreaks in the U.S.A. Poisoning from the *B. aertrycke* and Salmonella group used to be much more common than it been of late years. As might be expected, the majority of the outbreaks come from the small maker, the "back-room boys", whose material is often poor, consisting of milk that is just going off but the taint and taste of which is disguised by the freezing (in one U.S.A. case the resultant ice cream was found to contain 37,000,000 organisms per c.cm., about the same as sewage), whose factory is a small container sus-pended in a mixture of one part salt to ten of ice (21°), whose arms take the place of mechanical stirrers, and whose domestic flies roam with airy non-chalance from privy to person and from person to mix.

Steam sterilization of apparatus is essential and few small makers have that. Commercial ice cream should, in short, be like explosives, made only by fairly big concerns who give hostages in the form of expensive factories and laboratories, but even they cannot ensure the cleanliness of their itinerant vendors.

Incidentally, the disguising of taste by freezing, which anyone can demon-strate by comparing the taste of ice cream with its melted product, has been utilized in medicine. Children who cannot face milk can take ice cream: cod-liver oil loses much of its cloying fishiness when incorporated in it, and in the early days of liver therapy, when half-raw liver had to be devoured daily, it was found that it could be made fairly pleasant in a nut ice cream, I have no doubt that in children's hospitals it will be used as a vehicle for many medicines—a strawberry-sulphathiazole, a raspberry-ephedrine . . .

Its peculiar charm does not lie in the taste alone; the reception committee consists of the cold end-organs of the mouth and a selection of the hardier taste-buds. It is the anæsthetic effect of the cold and, probably the demulcent action of the gelatin and fat, that make ice cream such a desirable food, sometimes the only one that will be taken, in affections of the mouth and throat, aphthous stomatitis in children, for instance, and in quinsy.

To return to our bacteriology. Of course, the non-pathogens are much more numerous and are mostly of the lactic acid and coli-aerogenes groups, and from 2 per cent. to 22 per cent. of the latter have been found to survive pasteurization for thirty minutes at 145°. A high count may not be important in itself, but it shows there is something wrong somewhere. Curiously, a very low bacterial count in the milk is liable to give a tallowy taste to the ice cream. Other sources of bacterial contamination are the gelatin, the skimmed milk powder—whole milk powder is not nearly so liable to contamination, owing to its method of manufacture—and, as already mentioned, the dried eggs.

The cooling process which has brought our product down to 40° to 30° in half an hour and has been done by plate heat-exchangers is now ended and the next stage, one of masterly inactivity, is called "ageing".

(4) *Ageing.*—This consists of keeping the mix at about 37° for twelve to eighteen hours, and even at this temperature bacterial growth is not entirely stopped. Ageing increases viscosity and acidity, which is due to lactic acid and should not exceed 0.2 per cent. The weight at this stage is 9.25 pounds per gallon.

(5) *Freezing.*—The mix is now placed in a batch freezer and flavouring added, six ounces of vanilla, thirty-two ounces of coffee extract or calculated amounts of any other that is required. During the freezing process the flavouring is thoroughly whipped into the mix, so that the final ice cream weighs five pounds a gallon, that is to say nearly half of it is air, which has the disadvantage of destroying the remaining vitamin C. All the same, air is a necessary constituent, as without it the result would be a solid frozen mass.

The idea that freezing, even down to 18° and below, destroys bacteria is such a dangerous and damnable heresy that I feel impelled to lift the following from Harvey and Hill's "Milk Products" and display it like a placard.

(1) It has been demonstrated by Davis that hæmolytic streptococci remain alive in ice cream for at least eighteen days without any appreciable diminution in their virulence or number.

(2) Prucha and Brannan have found live typhoid organisms in artificially infected ice cream after a period of over *two years.*

(3) Wallace and Creuch, in 1933, demonstrated the fact that the *Salmonella enteritidis* and *aertrycke, Brucella abortus, Brucella melitensis* and *Bacillus tuberculosis* survived in ice cream for a period longer than three months.

Thus, and therefore, since sterilization is ruled out and pasteurization is

not entirely efficient, and freezing at the best merely perpetuates the *status quo* post-pasteurization, in the words of these authors "unless the raw materials are entirely free from blemish there can be no confidence in the finished product".

Apart from the main bogey of bacterial infection there are dozens of other accidents that may happen to ice cream in the making: milk that has been in contact with copper may give it a metallic taste; it may go "sandy", giving a gritty taste to the mouth, due to lactose crystals. A high fat content does not combine with a high sugar content and they have to be correlated with each other and with the various flavourings; prolonged storage destroys taste, and so on. In short, like most things well worth having it takes a lot of trouble to make, and the reason why it is well worth it, is that it is a first-class food which almost everybody likes.

SOME THERAPEUTIC ASPECTS

It is a most remarkable natural history fact that a frozen product, and because it is frozen it is not nearly so tasty, should appeal to about 98 per cent. of people. The clue to this problem lies, I think, in the fact that in children, this liking often amounts to a craving. There is a horrible story in the *Lancet* in 1940 about the girls of an English village being sexually corrupted by a mentally deficient ice cream man with his wares. Ice cream can be almost narcotic in its appeal. There is something in the icy substance surrendering to the body warmth as it passes from lips and tongue to pharynx, being forced reluctantly to give up its hoarded flavour that is represented in the cortex as a glow of triumph. To my mind there is no doubt that there is an element of atavism in this craving. It seems certain that the appreciation of cold by the mouth, pharynx and œsophagus, but not by the stomach, was an established mechanism long before man had fire. This mechanism accounts for the fact that if ice cream is eaten quickly it hurts. The head goes back, the spine is straightened, and the œsophagus does its heroic best to protect the stomach. Ice cream should be eaten slowly; but very little of it can be eaten quickly. Pain stops that and the sense of triumph fades. There seems to be no more danger of the gastric mucosa being frozen than of its being boiled.

In whooping-cough, children who vomit all other food will generally keep down ice cream, but whether this is due to stimulation of the cardiac sphincter, soothing of the gastric mucosa or some involved autonomic action, does not appear to be known.

So much for its acceptability, now for its intrinsic value. The word "ice cream" conveys no guarantee in this country; legislative control is inadequate and should at least provide for a minimum fat content and, more important still from a nutritive point of view, a milk-solids-not-fat minimum. Such a valuable product is well worth a law or two.

An analysis of ice cream based on three varieties of "bricks" in 1940 gave: water, 68.8 per cent., sugar, 17.5 per cent., protein, 3.9 per cent., fat, 13.2 per cent., starch, nil: value, 211 calories per 100 gm., about the same as in apple dumpling, fish cakes, baked kipper, stewed eels or boiled topside of beef. There is a useful amount of calcium and other minerals in the milk and milk powder as well as the milk vitamins, as is shown in the analysis of the following American helping, i.e., one-sixth of a quart: calories 200; protein 3.9 gm., calcium 0.131 gm., vitamin A (I.U.) 399, aneurin 0.038 mgm., riboflavin 0.105 mgm. The hundred pounds of ice cream with which we have been concerned gave 0.09 mgm. of carotene and 0.26 mgm. riboflavin per hundred gm., but no ascorbic acid could be found. Thus as a "vim" and vitamin giver, as well as a mine of useful minerals, ice cream is a paragon of virtue—her one little failing in the matter of vitamin C can be remedied by giving fruit juice or fruit with her, as in Pêche Melba.

One actual estimation of ice cream was 52.2 calories per ounce and 2.7 was immediately taken in melting it, but with the ices with a much lower calorie value this quick cooling effect has obvious uses in febrile conditions. Here we may turn aside for a moment to consider whether this body-cooling effect has any place in the heat catastrophes, when the working and climatic conditions are such that the body temperature rises inexorably and with little warning that it is running into thermal danger, until suddenly some chemical climax is reached which we call heat stroke or sun stroke, the essential point of which is that the heat-losing mechanism has failed and there has been an almost symptomless rise of body temperature. Obviously wind and water on the wide radiating and conducting skin, and bulkier water by the mouth and rectum, are the urgencies here, although water ices may play some small part later.

And that brings us to ice cream's poor relations, the mere ices, the thinnest of which, however, has its uses. A *water ice*, consisting of little more than water, a flavouring agent, and sugar, which may be glucose, is valuable after tonsillectomy and other post-operative conditions, as well as on those occasions when ice is traditionally used, such as in hæmoptysis.

I have seen a hospital in Canada where tonsillectomized children woke up to a bucket of it by the bed. It probably has an anæsthetic and hæmostatic effect. I had my tonsils removed nearly fifty years ago and, like many other people, still have a vivid memory of the faucial pain on waking, which as always with remembered pain has other sensory associates, in this case the taste and smell of blood and chloroform. Surely it is worth trying to assuage a memory so unpleasant that it can last a lifetime. Those who might scoff at the idea that small local alterations of temperature may have such lasting results may well contemplate the example of the experimental goat whose testicles were wrapped in cotton-wool and who consequently became sterile. Nature provides the biologically most important organ in the male

not only with a cremasteric radiator but with a tractile thermostat, so important can be small variations of temperature.

To turn from these thermal mysteries to the severely practicable. To make a more convalescent ice, a little more nutritious but still rather insipid stuff:—

Take milk, one gallon; sugar, one-and-a-half pounds; separated milk powder, nine ounces; best powdered gelatin, one ounce; vanilla extract to taste. The dry stuffs are mixed well together and stirred into the milk. Pasteurize at 155°F. and add flavour at freezer. In the absence of milk powder a custard type of ice may be made by using six ounces of cornflour instead of the milk powder and gelatin. Eggs may be added if available. The milk must be boiled and the cornflour, in the form of a smooth paste, cooked in it for a few minutes, sugar being added any time.

This is a much more solid affair than the other, and children, as usual, love it. With this base there seems to be considerable scope for the imagination, using grated carrot like nuts in the sundæs, including flowers like violets or rose petals, or primroses, which Disraeli said made "an uncommonly good salad", always keeping in mind the ice cream of one's dreams—a snowy perfection, hoarding warm, eminently scrunchable walnuts and flavoured with passion-fruit juice.

IN CONCLUSION

Finally, as the artists do, we may step back from our little canvas, become macroscopists as it were, people who bring great events down to the human eye, note man, the thermal animal, who is not directly dependent upon the earth's heat as the serpents are or partially dependent as the bats are, but by a hundred contrivances in lands that are cooler than he, and those that are hotter, proudly within a degree or two keeps the even tenor of his thermal way. Clearly, with our little pots of ice cream and ices we are not going to influence this hard-won, age-long status much; only for the moment and locally. Then we look at it from another angle. Ah, that's better. Man, the eater, who has this strange taste for frozen food, which may have a long history. This we can indeed use in such a way that the glorious fruits of the earth come without harm to those who most need them—the young and the sick.

THE EARLY RECOGNITION OF DISEASE

VII.—ORTHOPÆDIC DISABILITIES AND THEIR TREATMENT

By IAN LAWSON DICK, M.D., Ch.M., F.R.C.S.Ed.

AND SIR REGINALD WATSON-JONES, M.Ch.Orth., F.R.C.S.

From the Orthopædic and Accident Department, London Hospital.

"DOCTORS are too much concerned with the treatment of disease and too little with the maintenance of health." This unjust and misleading charge has been made by critics whose zeal for the advance of medicine has obscured their knowledge of the progress already being made. "Positive health" is the cry, but little thought is applied to the meaning of the words, or to the fact that positive health can be achieved only by the early recognition and treatment of disease, or indeed to the astonishing progress which has been made in this direction in recent years. In no branch of medicine is this illustrated more clearly than in the field of orthopædic and traumatic surgery, in which preventive methods play so important a part.

In 1928, from the first orthopædic clinic ever held in a certain North Wales area, thirty-six patients were admitted to hospital for difficult operations and long courses of treatment. Clinics were subsequently held at two-monthly intervals, and during the first few years many scores of patients were transferred to hospital with serious deformities and advanced disease.

One boy of eighteen was so twisted and dwarfed with the deformities of rickets that he had never stood or walked ; he could not even lie in a position of rest. Many children were so distorted that eight or ten operations were needed to osteotomize the femora and tibiæ at many levels before the limbs were reasonably straight. Adults with club feet which had never been seen by a medical man walked, not on the soles of their feet, but on the dorsal surfaces, which were protected with adventitious bursæ the size of tennis balls. One patient with right-angled flexion deformity of the knee and hip joints had walked on his hands and knees for twenty years. Congenital dislocations of the hip joint had never been reduced. Poliomyelitis had been allowed free rein in the development of contractures which are to-day unknown. Children with gross deformities had been hidden away by parents who, desperate with shame, never allowed them to see the light of day.

Go to the same clinic to-day and not one single patient will be found who needs urgent admission to hospital. Club feet are corrected within a few days of birth. Congenital dislocations of the hip joint are reduced during the first year. The ravages of poliomyelitis are controlled. Rickets is treated before deformities arise. Bow leg is cured by simple moulding. Knock-knee is not allowed to develop. Limbs are made to grow straight by simple shoe corrections. Supracondylar osteotomy of the femur which was performed in hundreds of cases by the pupils of Macewen and Robert Jones has virtually disappeared from the realm of surgery. We have not performed a single osteotomy of the femur for postural knock-knee in the last ten years.

JULY, 1946. Vol. 157   (57)

"Positive health" has been achieved; it has been achieved by the recognition of disease at so early a stage that deformity is prevented and disability relieved by simple corrective methods.

FLAT FOOT AND KNOCK-KNEE

The child who gains weight more rapidly than he gains muscle power stands with the feet in valgus; the muscles are unequal to their task; they give way and a valgus position of the foot and knee develops. If the position remains uncorrected the muscles continue to work at a disadvantage and they may never succeed in regaining normal balance. Moreover, if weight is borne constantly on a valgus foot, the bones grow in the shape of a valgus foot and as time goes on the mobile flat foot becomes a rigid flat foot. Similarly, if weight is borne through the knee joint in a valgus position the medial femoral condyle develops more rapidly than the lateral condyle and a fixed knock-knee deformity arises. Genu valgum steadily progresses and intermalleolar measurements show increasing separation at the rate of a quarter to half an inch every three months. Correction of the line of weight bearing can be secured by the simple device of raising the inner border of the heels and soles of the shoes a quarter of an inch. Valgus is thus corrected; the feet are inverted; weight is borne through the knee joint in a normal axis; and gradually the knock-knee grows straight. So constant is this relationship of the valgus foot to the valgus knee, and the varus foot to the varus knee, that by measuring intermalleolar separation at three-monthly intervals it is possible to judge the regularity with which crooking of the shoes is maintained. If deformity is increasing the surgeon knows that corrected shoes are never worn. If the deformity is stationary it is evident that crooked shoes are being worn but not with regularity; the child is sometimes allowed to walk in bedroom slippers or to stand barefoot on the bathroom floor. Only when the regime is maintained with rigid continuity, so that the foot is never put to the ground except in a corrected shoe, is the deformity rapidly and steadily corrected. In a growing child no other treatment is needed, even for as much as five to six inches of knock-knee deformity. Operations are unnecessary; irons, T-straps, and knock-knee braces are inadvisable; manipulations and forcible stretchings are definitely harmful.

CONGENITAL DISLOCATIONS OF THE HIP JOINT

There are three disorders of the hip joint in which successful treatment is almost entirely dependent upon early recognition. The first of these, congenital dislocation or subluxation of the hip joint, is a disorder of baby girls; the second, Perthes' disease or pseudocoxalgia, is common in children of both sexes; and the third, slipping of the upper epiphysis of the femur, occurs characteristically in adolescent boys. The usual textbook description

of all these conditions is that of the fully established deformity. The dislocated hip joint is said to be recognized by shortening and telescopic instability; but these signs are usually obvious only at so late a stage of development that the dislocation is irreducible. Pseudocoxalgia is described as coxa plana—a late stage of development in which there is flattening of the head of the femur and a mechanical misfit between the femoral head and acetabulum which must ultimately cause degenerative osteoarthritis. Slipped epiphysis is known as epiphyseal coxa vara because fixed deformity has arisen, the correction of which by forcible manipulation almost invariably causes permanent stiffness and arthritis of the joint. If these classical signs are awaited before the diagnosis is established, permanent disability is inevitable, and yet in each case there is no real difficulty in recognizing the disorder at so early a stage that perfect recovery is possible.

Early signs.—In North Italy, where congenital dislocations of the hip joint are much more common than in this country, the diagnosis is often made by medically untrained mothers during the first few months of the child's life. A watchful mother may detect asymmetry of the hips or broadening of the perineum. One of the most valuable of the early signs, easily recognized before the child walks, is asymmetry of the skin creases of the thighs. This inequality in the level of the transverse creases is almost pathognomonic of congenital dislocation and should never be ignored. Steps must be taken to secure radiological examination. At this stage the hip joint is subluxated but not completely dislocated. The only treatment needed is to strap a leather wedge between the lower limbs by which to hold the hips in wide abduction; the femoral head is thrust deeply into the acetabulum and the upper lip of the acetabulum, which otherwise is subject to the pressure of the displaced femoral head, grows normally. Perfect results may be secured without manipulation, plaster or operation.

It is not to be expected that in this country *congenital subluxation of the hip joint* will always be recognized during the first twelve months, but there should be no justification for failure to recognize it during the second twelve months when the child is walking. There is a very characteristic waddle in the gait. Normally when weight is borne on one leg the opposite side of the pelvis is raised so that body weight will be centred more accurately over the weight-bearing limb. But this is not possible if the hip joint is mechanically unstable. The pelvis then falls until it is held by the tension of gluteal muscles; instead of the pelvis being raised on the opposite side it is dropped, and this occurs with every step. The gait can be recognized a hundred yards away and no other sign need be elicited. Very often no other sign can be elicited: there is no pain; movements of the joint appear normal; telescopic instability is difficult to elicit and there may be no measurable shortening. If a baby girl walks with a slightly waddling gait the hip joints should at once be examined by X-rays. Reduction can usually be secured by simple abduction of the hips to the

right angled position; a "frog plaster" is applied and it is renewed from time to time over a period of twelve months. In many cases no other treatment is required, but X-ray examination should be repeated two or three times at monthly intervals after the plaster is first discarded, because the upper lip of the acetabulum may not have recovered fully from the effect of pressure of the femoral head during the first twelve months. If the acetabular ro has not developed fully, subluxation of the hip joint will recur and tl resulting incongruity of femoral head and acetabulum causes degenerativ arthritis after twenty or thirty years. In such cases a further period of protection in plaster is necessary, or alternatively a new upper lip of tl acetabulum may be constructed by operation. Every year that elapses make the recognition of congenital dislocation more obvious and the treatmen of the dislocation more difficult. When reduction is delayed beyond the ag of four or five years results are seldom perfect, and after the eighth or tent year congenital dislocations are usually irreducible.

Legg-Perthes' disease or pseudocoxalgia.—This disorder of the hip joir is due to impairment of blood supply of the upper femoral epiphysi: The vascular disturbance is sometimes due to obvious injury, such a fracture of the neck of the femur or traumatic dislocation of the joint, bu as a rule the onset is insidious and the cause of impairment of the bloo supply is unknown. If weight-bearing is permitted during the avascula phase, necrotic bone is crushed and the head of the femur becomes fla and broad. In due course the bone undergoes revascularization and th clinical signs disappear; the child may appear to be perfectly normal. Bu the effect of deformation of the head becomes obvious twenty or thirty year later; by then the joint is worn out and degenerative arthritis causes seriou pain and increasing stiffness. It is obviously important to protect the joir from weight bearing during the avascular phase, and if a normally rounde contour of the head of the femur is to be preserved the diagnosis must b established without delay.

The typical early clinical picture is that of a child, six or eight years old who for no obvious reason develops a painful limp. The pain may be ir the thigh and knee, and not in the region of the hip joint, because all three main nerve trunks of the thigh supply both the hip joint and the knee joint so that pain may be referred from one joint to the other. Clinical examinatior shows slight guarding of hip movements; there is muscle spasm and the hip may be held in a slightly flexed position. The signs resemble those of early tuberculosis of the hip joint but skiagrams do not show any destructive change. The epiphysis appears slightly dense, and in the later stages the texture of the bone is irregular and there may be an appearance of fragmentation. The child should be put to bed. It is often unnecessary to use traction, and abduction frames or plaster spicas are inadvisable. On the other hand, so-called "weight-bearing" calliper splints are unreliable. Bed rest should be

continued until revascularization is complete—usually within twelve months or two years of the diagnosis being established.

Slipped upper femoral epiphysis.—No disorder illustrates the importance of early diagnosis more clearly than that of slipping of the upper femoral epiphysis. Displacement of the epiphysis, which is in a backward and downward direction, seldom occurs as the result of acute injury; it is nearly always a gradual and insidious slipping which progresses almost imperceptibly.

An adolescent boy complains of pain in the thigh or knee and of a limp which lasts for a few days and then disappears as quickly as it came. For some weeks or months the limb appears to be perfectly normal, but painful limping recurs, only to disappear once more after a week or two. These attacks coincide with repeated minor displacements of the epiphysis, which in the course of a year or two becomes so far displaced that it lies on the back of the femoral neck, lodged in the digital fossa. By this time there is 90° of external rotation deformity and attempts to correct the displacement by manipulation under anæsthesia almost invariably stretch the ligamentum teres; thrombosis of the blood vessels within the ligament causes avascular necrosis, complete stiffness of the hip joint and a rapidly developing arthritis.

In advanced cases of adolescent coxa vara the penalty of stiffness and arthritis of the hip joint is so certain that no attempt should be made to secure reduction by forcible manipulation or operation. Serious rotation deformity may possibly be corrected by trochanteric osteotomy, but some degree of permanent disability must be accepted as inevitable. On the other hand, if the disorder is recognized at an early stage there is little difficulty in preventing further displacement and securing an almost perfect hip joint with no appreciable limitation of movement and no serious disability. Simple bed rest may be all that is necessary; in other cases light skin traction is required for two or three months. Epiphyseal fusion may be accelerated by driving a three-flanged nail through the neck of the femur into the epiphysis. But the fundamental point to be recognized is that by very simple measures the results of early treatment are excellent, whereas even with the most heroic surgical intervention the results of late treatment are deplorable.

Early recognition should present no difficulty. It is often possible to establish the diagnosis by the history alone. The simple fact that an adolescent boy complains of intermittent limping and pain in the thigh and knee indicates the probability of adolescent coxa vara. The patient often shows the rather fat and flabby physique of pituitary insufficiency. If it is found that although flexion movement of the hip joint is fairly free, internal rotation movement is limited, the diagnosis is confirmed. Early limitation of rotation cannot, however, be deduced simply by rolling the limb as the patient lies on a couch. The hip and knee should be flexed to the right angle and the lower leg used as the pointer of a protractor. Any restriction of the normal range of 30° internal rotation movement, and corresponding increase in the normal range of 60° external rotation movement, confirms that the

capital epiphysis has twisted backwards on the neck of the femur. In the later stages there is fixed external rotation deformity, which finally becomes so pronounced that the patient lies with the limb completely everted, the outer side of the foot flat on the bed and the patella pointing outwards. This is the stage when permanent disability is inevitable.

SCHEUERMANN'S EPIPHYSITIS OF THE SPINE

Scheuermann's disease was at one time known as the "rigid round back of adolescents". This name was in itself a confession of failure. There should be no deformity; the back need not be "round"; there need be no rigidity. The condition is one of obscure etiology in which there is disturbance of blood supply to the epiphyses of the lower dorsal vertebræ, probably analogous to the condition of pseudocoxalgia which has already been described.

Signs and symptoms.—Scheuermann's disease is often painless, not only in the early stages, but throughout its course. This important feature helps to differentiate it from tuberculous disease of the spine. Because the condition is painless it is often first noticed by a friend of the patient, a parent, or a teacher, rather than by the patient himself. The adolescent child is seen gradually to become more and more round shouldered and, unlike the deformity of simple postural kyphosis, it is most marked at the low dorsal level, and is increasingly difficult to correct. The diagnosis is confirmed in lateral skiagrams of the dorsal spine by the appearances which are characteristic of vertebral epiphysitis. The epiphyses at the upper and lower margins of the vertebral bodies show irregularity in shape and density and there is slight wedging of several vertebral bodies, usually the seventh, eighth and ninth. This appearance, the discreteness of the changes and the fact that several vertebræ are equally involved, serves further to distinguish the condition from tuberculous disease of the spine.

Treatment.—At this stage the tendency to increasing vertebral collapse and resulting deformity can be controlled by active back-raising exercises and by the wearing of a Thomas back support. In acute cases recumbency on a spinal frame or plaster bed is sometimes necessary for two or three months. In the early stages it is always possible to correct the deformity and thus to prevent the secondary changes of degenerative arthritis in the intervertebral joints, which in neglected cases causes rigidity.

ANKYLOSING SPONDYLITIS

Whether the incidence of ankylosing spondylitis is actually increasing, or whether the disease is now more often recognized in its early stages, a surprisingly large number of early cases seem to have come to notice during the years of war. If this is due to earlier diagnosis it is fortunate, for much can be done in the early case to mitigate the effects of this painful and crippling condition.

Diagnosis.—Ankylosing spondylitis is a disease of young adult males; it seldom occurs in women. There is a widespread arthritis which progresses to bony ankylosis of the affected joints. The disease occurs in three main forms. In each of these the first clinical signs are in the back and the first X-ray signs are seen in the sacro-iliac joints. Early radiological changes also occur in the symphysis pubis and in the manubrio-gladiolar joint of the sternum, but these are not of clinical significance. In the first form the disease is limited to the spine and sacro-iliac joints; in the second the hip joints are also involved; in the third the disease takes the form of a widespread polyarthritis. If it is untreated there is persistent pain in the back with increasing flexion deformity, so that ultimately the spine may become rigid in the shape of a C. The unfortunate patient's chin becomes fixed on his chest and he can look nowhere but at his own feet. In nearly two-thirds of the early cases X-ray therapy to the spine and the sacro-iliac joints produces dramatic relief in the symptoms and apparently complete arrest in the progress of the disease. Even in cases in which stiffness is not improved the pain is almost always relieved.

Treatment.—Flexion deformity of the spine may be prevented by lying at night without pillows, by resting for an hour or two during the day on a firm mattress in the supine position, by using a Thomas back support, and later by practising back raising exercises. In severe cases with more advanced deformity, recumbency in a plaster bed is advisable for a month or two. Successful treatment therefore depends upon early recognition of the disease; this fortunately is not difficult.

A young adult male complains of pain in the back of insidious onset and without injury or other obvious cause. He may complain of stiffness. When he tries to touch his toes it is seen that flexion movement occurs almost entirely at the hip joints. The lumbar and dorsal regions do not participate in the movement, and even in the stooped position the spine is rigidly straight. Involvement of the rib joints causes marked impairment of chest expansion; respiration becomes largely diaphragmatic.

Mistakes are often made at this stage because there is no radiological evidence of abnormality in the spine; not until several years later is there evidence of intervertebral ankylosis. Many unfortunate men with this disease have in consequence been labelled as neurotics or malingerers. There is actually no difficulty in establishing the diagnosis if the sacro-iliac joints are X-rayed. Blurring of the joint outline with loss of definition of the joint space and irregular sclerosis of the ilium and sacrum on each side of the joint are characteristic.

SPRAINS AND DISLOCATIONS

The very nature of most bone and joint injuries makes easy their recognition and an assessment of their probable extent and severity. Nevertheless, the "sprained" ankle, the "sprained" wrist and the "sprained" shoulder often cause permanent disability because the real nature of the injury is not recognized in the early stages.

The "sprained" ankle.—It was a common saying in "household" medicine that it was "worse to sprain an ankle than to break it", and this popular belief was based upon more than a grain of truth. A patient sustains a severe twist of the ankle and is seen later with a limb which is swollen and discoloured but in which the bony contours are found to be normal. X-ray examination shows no fracture or disturbance of joint relationship. The injury is therefore accepted as a sprain and simple measures of treatment are applied to reduce local swelling. Later, the patient finds that the ankle is "weak" and that if he walks on uneven surfaces it gives way and lets him down, so that he may even fall to the ground. There is recurrent pain and swelling. The fact is that this patient had not sustained a simple sprain but a complete rupture of the external collateral ligament of the joint. Failure to immobilize the torn ligament interfered with sound repair and left the joint permanently weak and unstable. Thereafter the joint subluxated momentarily every time the foot was inverted. The integrity of the lateral ligaments of a "sprained" ankle should always be tested specifically by X-ray of the joint under passive inversion and eversion strains, if necessary with a general or local anæsthetic. If the talus can be dislocated from the ankle mortice the injury is not a simple sprain but a ligament rupture which demands full protection in a walking plaster for not less than eight weeks.

Another injury which is often regarded as a sprain and in which failure to recognize the true nature leads to inadequate treatment and permanent disability is *fracture of the carpal scaphoid bone.* Far too often this injury is not diagnosed in the early stage. The failure of diagnosis is disastrous because if the fracture is treated promptly and efficiently it heals readily. In a recent series of 64 uncomplicated fractures of the carpal scaphoid bone, which were recognized within ten days of injury and were treated by prompt and complete immobilization in plaster, not one failed to unite by bone. If, on the other hand, the fracture is not treated promptly, non-union is almost certain, thus causing persistent pain in the wrist, weakness of grip and ultimately osteoarthritis of the joint. There are two important reasons why fracture of the carpal scaphoid bone is difficult to recognize in early X-rays. The scaphoid lies obliquely in the carpus, and routine antero-posterior and lateral views of the wrist do not show it in profile. To do this it is necessary to take oblique views. At least four projections of the joint are essential for complete X-ray examination of the carpal scaphoid bone— postero-anterior, lateral, 45° of pronation, and 45° of supination. The fracture may be seèn in one only of these projections, the other three not showing any sign of injury. Secondly, the fracture line may be faint and indistinct, and it may be necessary to examine the films closely with a lens before a slender breach in continuity of the bone is recognized. After a week or ten days, hyperæmic decalcification of the bone makes the fracture line more obvious. Any patient, especially a young man between the ages of fifteen and thirty, who injures his wrist by a back-firing engine or by a fall on

the outstretched hand, and who complains of pain on the radial side of the joint with tenderness on pressure in the anatomical snuff-box, must be presumed to have sustained a fracture of the carpal scaphoid bone. Simple sprain of the wrist is one of the most rare of injuries; this diagnosis should be accepted only if good quality films, repeated after an interval of ten days, do not show any evidence of fracture.

Dislocation of the shoulder joint.—It is now generally recognized that, in order to minimize the tendency to recurring dislocation, the shoulder joint should be immobilized after reduction of a dislocation. The limb should be strapped to the chest over a small axillary pad in the position of adduction and internal rotation. There is, however, one notable exception to this rule. If the dislocation is complicated by rupture or avulsion of the supraspinatus tendon the shoulder must be immobilized in abduction and external rotation in order to prevent the serious disability which follows unsound healing of this tendon. Avulsion of the tendon is readily recognized in antero-posterior skiagrams by the flake of bone which is displaced upwards from the greater tuberosity; but a tear of the tendon can be recognized only by clinical demonstration of the fact that the normal scapulo-humeral rhythm of abduction of the shoulder is disturbed. Abduction movement is normally initiated by the humerus moving on the scapula; rotation of the scapula itself occurs later in the range of abduction. When the supraspinatus tendon is torn the normal mechanism for fixing the head of the humerus in the glenoid during abduction is lost, and the patient attempts to abduct his arm by shrugging the shoulder and elevating the scapula. Scapulo-humeral rhythm should always be examined immediately after the reduction of a dislocation of the shoulder, lest the disabling complication of a tear of the supraspinatus tendon should pass unrecognized and thus cause permanent weakness and loss of abduction movement.

CONCLUSION

This review of certain disorders of joints, diseases of bones, deformities of the spine, and injuries of bones, joints and tendons, is far from comprehensive, but it illustrates the importance of early recognition and early treatment of disease. Preventive treatment is an essential feature of the management of disabilities of the limbs and spine. This branch of medicine is known as orthopædic surgery, but it is better described as "orthopædics", because surgical intervention plays a small and relatively unimportant part. It is true that in former years many serious deformities necessitated difficult and complicated operations, but since that time great progress has been made in recognizing disease and injury at so early a stage of development that it is amenable to simple corrective measures, to manipulation, exercise or the temporary use of appliances. Early diagnosis is the key to continued success, and for this every orthopædist is dependent upon the general practitioner of medicine.

REVISION CORNER
OPHTHALMIA NEONATORUM

THE view generally held that ophthalmia neonatorum is synonymous with gono-coccal ophthalmia is erroneous. Although there are differences in detail, most series of cases of ophthalmia neonatorum show that the affection is produced by a great variety of organisms, and in many series the gonococcus is not the predominant causal organism. It was responsible for about 25 per cent. of 737 cases seen at the ophthalmia neonatorum unit at White Oak Hospital between 1939 and 1945. *Staphylococcus aureus* accounted for about 35 per cent. of cases, whilst the meningo-coccus, pneumococcus, streptococcus, and other coccal organisms each contributed a small percentage. Bacilli were responsible for about 20 per cent. of cases, diphtheroids being the most common, but the Koch-Weeks bacillus was not a curiosity as a causal organism.

Recent series, like the older series, contain some 10 to 20 per cent. of cases in which no micro-organism can be found in the smear or culture. Most of these "negative" cases do not represent faulty bacteriological examination, as was once thought, but are examples of ophthalmia neonatorum due to a *virus infection.* This virus has not been isolated in culture, but its existence has been demonstrated by animal inoculation, and by the presence of inclusion bodies in the conjunctival epithelium—a finding responsible for the designation of inclusion ophthalmia neonatorum, or inclusion blenorrhœa. The incubation period of inclusion blenorrhœa is generally 6 to 12 days (instead of 3 to 5 days in bacterial ophthalmia neonatorum). In other respects inclusion blenorrhœa is clinically identical with other types of ophthalmia neonatorum. Inclusion blenorrhœa is part of a clear-cut venereal disease. In the mother of the affected baby a scraping of the epithelial cells taken from the transitional lining at the os of the cervix generally also shows *inclusion* bodies. To complement ophthalmia neonatorum in the baby and inclusion cervicitis in the mother there is the nonspecific urethritis in men in which inclusion bodies can also be demonstrated in epithelial scrapings. This virus infection seems to be *fairly widespread in the community; it gives minimal clinical symptoms, and* not infrequently it is subclinical.

PROPHYLAXIS

The *essential measure of prophylaxis* in ophthalmia neonatorum is the treatment of maternal infection during pregnancy. In the light of present knowledge this means more than the treatment of active or chronic gonorrhœa, or even of leucorrhœa. Ophthalmia neonatorum will be eliminated only when maternal infections are eliminated.

The more *immediate method of prophylaxis* associated with the name of Credé is immensely valuable, but has distinct limitations. The mechanical part of the procedure—cleansing of the lids as soon as the head is born and before the baby is allowed to open its eyes, and care being taken to prevent any contaminated bath water reaching the baby's eyes—is now part of the routine of delivery, and is consistent with the principles of asepsis. The chemical component of the procedure, the instillation of silver, or some other disinfectant into the eye, is of doubtful value and is a relic of Listerian antisepsis. It is a moot point if an infected conjunctival sac will be disinfected by the application of one drop of an antiseptic. There seems to be no reason for using silver nitrate, which is far from foolproof. There is nothing to indicate that it is superior to the organic silver preparations, which at any rate are innocuous. If anything is to be put into the baby's eyes it is best to put in two or three drops of 20 per cent. argyrol, rather than 1 per cent. silver nitrate. There is nothing to be said for drops of sodium sulphacetamide ("albucid"); they are largely ineffective locally. Nothing as yet is known of the value of penicillin as a disinfectant of a presumably infected surface.

TREATMENT

The classical methods of treatment have to-day no place in the treatment of ophthalmia neonatorum. Those methods consisted essentially of ceaselessly washing away all the pus from the infected eye to prevent the pus from damaging the cornea, and waiting for spontaneous healing, which generally took some weeks. Such adjuvants as were used—antiseptic drops and occasionally shock therapy by milk injections—probably had little effect on the infection. The classical methods of treatment therefore did little more than prevent complications. Their value against the infection itself was always problematical.

In contrast, the modern methods of treatment deal with the infection primarily. Two alternative procedures are available:—

(1) *Sulphonamide therapy.*—Employed locally the sulphonamides are useless in ophthalmia neonatorum, as they are inactivated by pus and break-down products of the tissues: given by mouth they are highly effective. When the baby is first seen a swab of the pus is taken both for a smear preparation and for a culture. The eyes are then irrigated with bland lotion, such as half-normal saline solution at room temperature; 1 per cent. atropine sulphate drops and drops of medicinal paraffin are instilled as a routine measure, and half a tablet of sulphamezathine (0.25 gm.) crushed into powder is given by mouth in a teaspoonful of water or milk. Sulphamezathine administration is continued in doses of 0.125 gm. every four hours, day and night, until forty-eight hours after a clinical cure is obtained. Local treatment consists in three-hourly irrigation with a saline solution during the first day in cases with profuse discharge; as a rule there is no need for further irrigation on the subsequent days. After irrigation, medicinal paraffin is instilled as a precaution against the sticking together of the lids. Atropine is instilled three times daily in cases with corneal haze or ulceration.

With this treatment, swelling of the lids generally subsides within twelve hours after admission; purulent discharge disappears within twenty-four hours, so that a threatening purulent ophthalmia becomes a simple conjunctivitis giving no anxiety. The eyes are either dry or very nearly so within seventy-two hours.

The dreaded corneal complications of ophthalmia neonatorum do not develop. Some 40 per cent. of all babies show complete clinical cure within three days, and 90 per cent. are cured within eight days. Such cases as are resistant to treatment are only relative failures with a somewhat prolonged course which, however, does not give rise to anxiety, as there is conjunctivitis rather than purulent ophthalmia. Isolated cases of complete resistance to sulphonamides have, however, been observed. Babies tolerate oral sulphonamides well. Nothing is gained by using doses smaller than those indicated, and it is important to continue the sulphonamides for forty-eight hours after clinical cure, as the too early suspension of treatment may lead to a relapse.

(2) *Penicillin therapy.*—Unlike the sulphonamides, penicillin remains effective in the presence of pus. It can therefore be used as a local agent, and has one other advantage over the sulphonamides in that cure is even more rapid and dramatic. For the present, however, treatment is rather exacting, and it is not yet as standardized as oral sulphonamide therapy.

In the use of penicillin, concentration and frequency are all-important. The routine procedure now in use at White Oak Hospital consists of the following stages:—

(1) A swab of the pus is taken for bacteriological examination.

(2) The eye is then irrigated with half-normal saline at room temperature to wash away the pus.

(3) A nurse seated on a chair takes the baby on her lap, and another nurse is responsible for putting in two drops of penicillin, 2,500 units per c.cm., every minute into the eye.

(4) Pus does not tend to reform while this treatment is in progress. Any secretion formed can readily be wiped off with pledgets of cotton-wool.

(5) Within twenty to thirty minutes the picture is changed. Although the lids are still swollen, and the conjunctiva still remains moist, there is now no tangible secretion.

(6) After thirty minutes of this treatment the baby is returned to its cot. One drop of atropine 1 per cent. is instilled as a precautionary measure.

(7) Penicillin drops are now continued at five-minute intervals for half an hour.

(8) At the end of this half hour penicillin is continued at half-hourly intervals for six hours, and subsequently at hourly intervals for twelve hours. By this time the eyes are as a rule normal.

Failures with local penicillin treatment, as with oral sulphonamide therapy, are few. In such cases these two agents may be used in combination.

A striking feature of both sulphonamide and penicillin treatment is their efficiency over the whole range of causal organisms, including the virus of ophthalmia neonatorum. Gonococcal cases respond rather more quickly than non-gonococcal cases to oral sulphonamide treatment, and it is possible that those due to diphtheroids respond rather less readily to local penicillin therapy than the cases due to other organisms. These, however, are minor differences and do not materially affect the dramatic and gratifying response of ophthalmia neonatorum to the modern methods of treatment.

For a full discussion see:—Sorsby, A. (1945): "Ophthalmia Neonatorum", London. PROFESSOR ARNOLD SORSBY, M.D., F.R.C.S.

THE TREATMENT OF ACUTE OTITIS MEDIA

THERE appears to be a general impression that the sulphonamides have solved the problem of acute otitis media and that the operation for an acute mastoid is no longer needed except when the sulphonamides have not been used or have been misused. It is a fact that before the advent of chemotherapy approximately 80 to 90 per cent. of cases of acute otitis media recovered completely if they were reasonably treated. By this is meant myringotomy, when there was pus in the middle ear, rest in bed while the temperature was raised, and adequate aural hygiene. Various series of cases of acute otitis media treated with sulphonamide have been published and the impression gained is that approximately 10 to 12 per cent. of all cases treated require a mastoid operation. These two observations do not indicate a revolution in the prognosis.

CHEMOTHERAPY

Two questions arise from considering the problem of treatment. Should sulphonamides be used? and if so, what should be expected of them?

The views I am now expressing are personal views, and many may disagree with them. In 1945, at a meeting of the otological section of the Royal Society of Medicine, I stated that sulphonamides were not indicated in the treatment of acute otitis media. At that time I was a service medical officer and could treat all cases of acute otitis media in hospital under my own supervision, with adequate nursing facilities. Under these conditions I came to the conclusion that those patients who were going to get better could get back to duty more quickly if sulphonamides were withheld, and that in those in whom a mastoid operation was indicated the situation became clear more quickly, and the operation was therefore performed sooner, if sulphonamides were withheld. Further, I concluded that sulphonamides did not decrease the number of patients requiring mastoid operation. These conclusions remain unaltered by my civilian experience. But the advantages of chemotherapy which were unimportant to a Service medical officer are most important to the civilian practitioner, and in civilian practice outweigh the disadvantages. These advantages are that chemotherapy reduces all the symptoms rapidly and with

reasonable certainty. The temperature falls, the pain decreases, and the otorrhœa, if present, becomes less profuse or dries up. Thus home treatment is attended by less excitement. The practitioner prescribes the tablets and the patient's condition improves; and in nine out of ten cases a complete cure is affected. This sequence of events is satisfactory to both patient and practitioner, and I have therefore revised my opinion and consider that chemotherapy is indicated in the treatment of acute otitis media. It must be emphasized, however, that whether the ear is going to need a mastoid operation or not the symptoms will be reduced, and thus a careful watch must be kept on the patient to detect the reduced symptoms, otherwise, in a small proportion of the cases, the result of treatment will be highly unsatisfactory.

SURGICAL INTERVENTION

The object of treatment in otitis media is to finish with a live patient with an intact tympanic membrane and normal hearing. If sulphonamides are to help in attaining this end the small symptoms and signs must be carefully observed and operation performed in the necessary cases without undue delay, otherwise the hearing will not be normal at the completion of treatment. A typical picture of the patient treated with sulphonamides and requiring a mastoid operation is as follows:—

Two to three weeks previously the patient had severe earache and a high temperature. Adequate dosage of sulphonamide was started immediately. The temperature and pain were both rapidly reduced and the patient appeared convalescent in three or four days. The sulphonamides were discontinued in five to six days. However, the temperature was not normal, it rose to 99 or 99.5° F. in the evenings, perhaps only every second or third evening. The tympanic membrane did not regain its normal lustre or colour, a slight blush persisting. By the end of the third week a slight sagging of the deep postero-superior meatal wall can be detected. The hearing remains subnormal, although not very bad, but the loss is detectable by sickroom methods. There is probably slight tenderness over the mastoid tip and antrum. None of these signs is obvious except perhaps the mastoid tenderness, but they are the only clinical signs of the mastoid infection until a complication of the acute mastoid develops.

If these signs, slight pyrexia, slight abnormality of the tympanic membrane, slight loss of hearing and slight mastoid tenderness, persist into the third week, mastoid operation should be considered. Confirmation can be obtained by radiology of the mastoid, which will show loss of translucency of the cells and slight blurring of the cell outlines. The two questions posed may thus be answered. First, sulphonamides are indicated in the treatment of acute otitis media. Secondly, they will reduce the anxiety of patient and relatives but call for increased vigilance by the practitioner, as they reduce the prominence of the signs which indicate surgical treatment of the mastoid.

GENERAL SCHEME FOR TREATMENT

Working rules may be suggested as follows:—*Sulphadiazine* or *sulphamerazine* (neither causing nausea), should be prescribed in full doses, according to the age and size of the patient. Full dosage should be given, as small doses at long intervals are bound to be totally ineffective. and the idea that a slight infection can be cured by a small dose is fallacious. Sulphadiazine is used in the same doses as sulphapyridine. Adults should be given an initial dose of 2 gm. and a maintenance dose of 1 gm., four-hourly; the 2 a.m. dose may be omitted if a double dose is given at 10 p.m. The dosage depends upon weight, so that children under twelve should be given a half dose, and infants a quarter dose. If it is desired to work out the dose for children accurately, the initial dose recommended is 1 gm. per 20 lb. of body weight and the maintenance dose is 1 gm. per 15 lb. body weight per day, divided into six four-hourly doses. Sulphamerazine is more slowly excreted and the adult dose is 2 gm. initially and 1 gm. eight-hourly. For children under 60 lb. body weight the initial dose is 0.5 gm. and the maintenance dose 0.5 gm. per 10 lb. body weight per day, divided into three equal eight-hourly doses.

If the earache and bulging of the membrane persist after twenty-four hours, *myringotomy* should be performed. The chemotherapy should be continued until

the temperature has been strictly normal for forty-eight hours or until an adequate total dose has been given. It is not usual to continue the chemotherapy for more than seven days. After seven days a thorough examination is carried out and if any abnormal physical signs persist a further examination is carried out in fourteen days. If any aural signs or symptoms persist after fourteen days the mastoid should be examined radiologically and the question of mastoid operation considered. The details of the indications for operation cannot be discussed here. To operate is a difficult decision to make, but unless surgeons are prepared to operate at the end of three weeks on very small signs the use of chemotherapy will increase the residual deafness after mastoid operations. The acute ears which are treated by chemotherapy and are subjected to a mastoid operation after about three weeks have a good prognosis, and it is not unusual to have a soundly healed wound, normal hearing and an intact tympanic membrane three weeks after the operation.

It may be added that, so far as can be judged at present, acute otitis media treated with *penicillin* behaves in the same manner as when treated with sulphonamides.

GEOFFREY H. BATEMAN, B.M., F.R.C.S.

THREADWORMS AND TAPEWORMS
THREADWORMS (ENTEROBIASIS)

A SUGGESTION of enterobiasis as the cause of long-continued anal pruritus in an adult is likely to meet with the objection that no threadworms have been seen in the fæces. It is a fact, however, that if this nursery method of diagnosis is relied on, most cases of infestation in the adult will be missed. Pruritus—actually a tickling—begins after the subject goes to bed, increases as he becomes warmer, and dies away in the early morning when egg-laying has ceased. If felt at all during the day, it is no more than a reminder of what awaits the victim later. The nightly torture and loss of sleep bring about a nervous state of depression and irritability, often aggravated by acute self-pity. Various reflex phenomena may be prominent—gastric hyperacidity and its train of symptoms, frequency of micturition, and the interesting itching of the nose. Excessive secretion of intestinal mucus may make an anal pad a necessary precaution. Appendicular colic and appendicitis are sometimes set up. Invasion by the vagina may lead to salpingitis. Not infrequently the patient seeks advice for some secondary development, and makes no mention of pruritus.

Diagnosis.—Every case of nocturnal pruritus ani should be investigated as possible enterobiasis. Each female deposits about 11,000 eggs. The eggs may be recovered in scrapings of the perineum, or by dabbing with adhesive cellulose tape: they are rarely found in the fæces. In adults it is preferable to demonstrate the worms by a rectal wash-out, self-administered when pruritus is at its height. A child's enema-bulb is satisfactory and safe, the patient refilling it several times while remaining lying down with the buttocks raised. Use kitchen salt, 2 tablespoonfuls to a pint of cold water. The enema is retained for a few minutes, the patient making repeated changes of position, and then passed into a vessel for examination. If threadworms are responsible, pruritus stops instantly and does not return that night. This in itself is almost diagnostic.

Treatment.—Similar wash-outs are given nightly when pruritus is active. The patient adopts this simple procedure eagerly when he finds that it ensures uninterrupted sleep, a luxury unknown perhaps for years. To kill young worms in the small intestine and cæcum, give helminthics by the mouth. Gentian violet in enteric-coated capsules, 1 grain t.i.d. before food (children, a daily total of 0.15 grain, in divided doses, for each year of apparent age). Continue for eight to ten days, and after a week, repeat. Or, hexylresorcinol in capsules, 1 gm. (children, 0.6 to 0.8 gm.), taken on an empty stomach in the morning; fast six hours and wash out the rectum. The dose may be repeated after three days. Hexylresorcinol may be given as an enema, 1 : 2,000, 2 pints for adults; for children, whatever quantity can be

tolerated without discomfort. This may be repeated after three weeks. Intestinal mucus inhibits the drug.

A cure cannot be hoped for if reinfection by the mouth continues, and if this were stopped for good the infestation would die out of itself in about six weeks. The hands must be well washed every time the body or underclothes have been touched, because of the wide dispersal of eggs. If the patient is told to imagine that his skin and underclothing have been soaked in strong poison, any trace of which conveyed to the mouth would cause instant death, he will follow his instructions more intelligently. A return of pruritus which had seemingly ended indicates some flaw in the preventive routine, two to three weeks previously.

Although children, for obvious reasons, readily infect one another, it is a curious fact that an adult may remain infected for years without transmitting the parasites to any member of his family or household. Finally, a diagnosis of non-symptomatic enterobiasis should not be accepted unless the worms are recovered and properly identified.

TAPEWORMS (TÆNIASIS)

Human intestinal tæniasis is usually unsuspected until segments are noticed by chance. If longer than broad, for practical purposes they may be taken as those of either *Tænia solium* or *T. saginata*, the latter the commoner and more resistant species. Sometimes segments of *T. saginata* emerge from the intestine by their own locomotive power, and wander about outside, to the host's discomfiture. They may enter the stomach and be vomited. Occasionally in *T. solium* infestation, all segments are passed in a partially digested state and can be recognized as segments only under the microscope. There may be no appreciable symptoms; other patients complain of gastric or abdominal discomfort or of diarrhœa. Sometimes the appetite is voracious. There may be nervous irritability and depression, symptons likely to be intensified when the parasite is discovered, or they may date only from its discovery. A low degree of eosinophilia is usual.

Diagnosis.—Identify the species without delay. In *T. solium*, the uterus, seen as a longitudinal line, gives off eight to ten branches on each side; in *T. saginata*, eighteen to thirty. Wash a fresh segment in water, press between two slides, avoiding contamination of the hands, and count against the light, using a hand lens. The eggs of the two species are indistinguishable. If the parasite is *T. solium*, isolate the patient and take every possible precaution to guard against his swallowing eggs and thus contracting cysticercosis, or transmitting eggs directly or indirectly to others. Each mature segment contains about 40,000 eggs.

Treatment.—Liquid extract of male fern in capsules, three 30-minim doses (if the case is a recurrence, four such doses) at intervals of twenty minutes, followed by oil of turpentine 30 minims in emulsion after a further twenty minutes: one hour later, magnesium sulphate, ½ an ounce. Or, the liquid extract in two 60-minim doses, one hour apart, followed by a saline purge two hours later. As preparatory treatment: fluid diet including glucose, for three days, the bowels being well opened during this period; no breakfast, except tea or coffee, on the morning of treatment. The patient remains lying down until purgation begins. The worm is expelled more readily if the patient is seated on a vessel containing warm water, as recommended by Celsus. Failure may result from using a preparation itself not fresh or from long storage of male fern before extraction. Trichlorethylene (or carbon tetrachloride) 3 c.cm. and oil of chenopodium 1 c.cm. in capsules (or given together in 1 ounce of liquid paraffin), followed by a saline purge three hours later, may be effective. Except for the omission of breakfast before the dose, dieting is unnecessary. A course of glucose and calcium given beforehand is said to counteract ill-effects. Treatment has not necessarily failed if the head is not found. If it survives, segments reappear, generally in three to four months.

LIEUT.-GEN. SIR WILLIAM MACARTHUR, M.D., F.R.C.P.

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and despatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Cerebral Diplegia

QUERY.—I have a patient, aged fifteen years, with cerebral diplegia. His mental condition is normal. He has a spastic gait. The arms are also affected. Can anything be done to improve his walk? Both legs are approximately the same length, so surgery is out of the question.

REPLY (from a neurologist).—As cerebral diplegia is due to irreversible damage to the cerebral hemispheres, treatment consists in assisting the patient to make the fullest use of whatever power is left to him, either by physiotherapy or by operative measures. As the patient is of normal mentality, and presumably co-operative, remedial exercises for the legs are indicated. Active movements of the legs in a warm bath, regular and full passive movements of the hips, knees, and ankles, and walking exercises under supervision (with footsteps marked on the floor) should be practised daily. Psychologically, the aim and attainment of a goal is an added incentive. The fact that the legs are of equal length does not veto operative treatment. The latter should be reserved for those cases with severe spasticity, contractures, or deformities. Severe spastic adduction at the hips, contracture of the hamstrings, and inability to put the heel on the ground due to spastic or shortened calf muscles, are some of the indications for possible surgical treatment, which latter includes the lengthening of tendons, e.g., the tendo Achilles, section of the adductor tendons of the hip, or section of certain peripheral nerves, as described by Stoffel. Other operative measures have been tried, but with little success. Careful assessment of the individual case is needed before surgical operation is considered. Operative treatment is, of course, palliative, and can have no direct effect on the damaged cerebral hemispheres.

Premature Ejaculation

QUERY.—In my practice, which is in the southern part of Iraq, I have recently seen several cases of sexual impotency which I find difficult to treat. These male persons are mostly young, average age twenty-five years, healthy, sexual organs normal, and have had intercourse previously, but on meeting their wives for the first time no erection occurs, or ejaculation takes place before the real act and maximum erection. Locally they call such persons "locked persons," i.e., a person had locked the man and he cannot have intercourse with his wife unless the same "locker" will unlock him. I do not believe in such things, but such cases are present, and I have treated them psychologically and by giving them some aphrodisiacs, but without any results. Will you kindly explain the cause and treatment of such cases?

REPLY.—The local term "locked person" is by no means a bad description of these cases of premature ejaculation. But what is not recognized locally is that the "locker" is not another person but the patient's own subconsciousness. Premature ejaculation is, of course, the commonest difficulty experienced in early married life. It is caused either by anxiety, or, as many psychologists believe, by the patient's not having fully committed himself to intercourse with his wife. Because this is the case, he escapes from it by having an ejaculation. Many cases respond to reassurance that there is no physical disability, combined sometimes with the giving of an antispasmodic (eserine), or even a little bromide. But some can only be cured by prolonged psychotherapy. They are amongst the most difficult cases of sexual disability that have to be treated. Any treatment that has a strong suggestive action will, however, be helpful.

KENNETH WALKER, F.R.C.S.

Blood Cholesterol in Disease

QUERY.—What are the essential causes of fluctuations in the levels of the blood cholesterol in disease? What are the causes of hypercholesterolæmia and hypocholesterolæmia, and what are the normal limits for cholesterol in the blood?

REPLY.—Cholesterol in plasma or blood is determined by various modifications of Bloor's method, which itself is based on Liebermann's colour reaction for cholesterol. Cholesterol esters with fatty acids, which normally amount to about 60 per cent. of the total cholesterol, are included in the reaction and have the modifying effect that the colour develops more rapidly and fades more rapidly with esters than with the cholesterol itself, which is used as the standard for comparison. This source of error, and the incomplete extraction of the material which may occur, operate mainly in reducing an already low result. The mean figure for cholesterol in serum or plasma in adults is about 200 mgm. per 100 c.cm. Cholesterol is subject to so many influences that it is difficult to say what are the normal limits, but no conclusion other than normality can be drawn from figures between 180 and 220 mgm., and

on the high side figures below 300 mgm. are not at present of much significance. Figures as low as 80 mgm. and as high as 800 mgm. have been obtained.

In *jaundice*, low cholesterol signifies failure of hepatic function and high cholesterol biliary obstruction, but the processes may be combined so that the cholesterol may be within normal limits. If the cholesterol has been high and proceeds to fall gradually this may signify disappearance of the obstruction and therefore of the jaundice, or may mean hepatic failure with persistence of the jaundice.

In *thyroid disease* a hyperthyroid condition is accompanied by a low cholesterol, but the figure is not usually below 140 mgm. The cholesterol is not always low in thyroid enlargement nor is it always in agreement with basal metabolism, and a further study of the discrepancies may lead to useful conclusions. When the cholesterol is low to start with, it rises in treatment with thiouracil and may be a useful guide to dosage. In thyroid deficiency the cholesterol may be as high as 500 mgm. and falls when thyroid is given. As a guide to dosage, cholesterol has the advantage over basal metabolism determinations in that changes are slower and less subject to daily variation.

In *nephrosis* the cholesterol is high, and may be high apart from lipæmia, whilst in uræmic nephritis the cholesterol is usually normal, although the conditions may be mixed.

In *diabetes* high cholesterols appear to be confined to cases with lipæmia and have no bearing on the condition of the generality.

Cholesterol has been found high in *psoriasis* but the average of results does not depart largely from the normal.

In *cholelithiasis* high cholesterols, when they occur, are probably dependent upon the associated hepatic disturbance

In *pregnancy* the matter requires further study and a slightly raised cholesterol may have no more significance than the rise in cholesterol that takes place in a normal person in the earlier stages of starvation.

J. H. RYFFEL, B.CH., B.Sc.

Penicillin in the Treatment of Gonococcal Urethritis and Prostatitis

QUERY (from a reader in Cyprus).—All articles and notes which I read about the treatment of gonorrhœa refer to acute cases of urethritis. For this reason I should be grateful for an opinion on the treatment with penicillin of chronic gonococcal urethritis and prostatitis with moderate urethral discharge especially detectable in the early morning. Can penicillin alone eradicate gonococci without other measures? I tried this treatment twice, with 200,000 units of penicillin, without any result.

REPLY.—Assuming that the chronic urethritis and prostatitis are really due to gonococci and not to infection by some organism that is resistant to penicillin, it would be expected that the administration of penicillin in adequate dosage would materially help towards the eradication of the infection, and, indeed, is often all that is required. Failure of the penicillin to bring about a cure without other measures might be due to the gonococci being penicillin-resistant, but a more likely explanation would be that the remedy had failed to reach the gonococci in some or all of the foci in sufficient concentration. This might be remedied by repeating the penicillin treatment with much larger doses—in such a case I have sometimes given 700,000 units in a single injection, with complete success—or by searching for the foci and making them drain by methods described in the textbooks. Naturally drainage of foci would be supplemented by administration of penicillin and/or appropriate sulphonamides.

COL. L. W. HARRISON, C.B., D.S.O., M.B., F.R.C.P.ED.

Splitting of the Finger Nails

QUERY (from a reader in Malta).—A female patient of mine, aged twenty-seven, married, and with two healthy children, suffers from splitting of the finger nails into two layers. This is a serious inconvenience as the nails have to be cut quite short. The splitting extends the whole width of the nail, but only the free portion seems to be involved. She is otherwise healthy. She uses nail paint or polish only very seldom. Can you suggest the cause and treatment of this condition?

REPLY.—There are two possible causes of the splitting of the finger nails into two layers: (1) a local one due to the application (even occasionally) of nail paints or varnishes, or to the finger tips being immersed in some acid fluid, e.g., working with the juice of citrous fruits; (2) failing the above causes I have seen numerous cases of splitting of the nails due to a toxic absorption from some focus of infection in connexion with the tonsils, teeth, accessory sinuses, or appendix. The most marked case I ever saw occurred in a medical man who had an encysted appendix abscess. After the abscess was opened and drained all the nails dropped out and grew in again in a normal condition. The treatment, naturally, is to find the cause and remove it. No local application to the nails is of any use.

R. CRANSTON LOWE, M.D., F.R.C.P.ED., F.R.S.E.

PRACTICAL NOTES

The Bleeding Nipple

IN a symposium on cancer of the breast, O. J. Campbell (*Surgery*, January 1946, **19**, 40) discusses the problem of the bleeding nipple. He is of the opinion that whilst "bloody discharge can never be overlooked or ignored until cancer has been ruled out . . . too much fear, even panic, has been exhibited toward the symptom of bloody discharge from the nipple". Diagnosis is essentially a problem for the pathologist, and frozen sections should not be relied upon. Time must be allowed for the preparation and examination of permanent slides. In the absence of a palpable tumour, three diagnostic measures are useful in localizing the site of bleeding: (a) transillumination, (b) mammography, and (c) pressure tests. These last are carried out by point pressure by the finger on various segments of the areola. In a series of fifty-five cases, thirty-three were non-malignant: nineteen patients with duct papillomas, thirteen with cystic disease and one with dilated ducts only. Of these thirty-three patients, in twenty-three (69.6 per cent.) the breast was saved, either local excision or segmental resection being carried out. Stressing the importance of saving the breast in young women, Campbell gives the following guides for treatment in younger women:—When the source of bleeding cannot be localized, when it is intermittent, recurrent or involves a number of ducts, and no palpable tumour exists, removal of the breast is not justified. Similarly, local excision is sufficient when the source of the bleeding is due to adenocystic disease, even though the remainder of the breast may harbour the condition. The risk of malignant change in adenocystic disease does not justify amputation of the breast except in later life, when the loss of a breast is less of a tragedy; in these older patients amputation may be considered if the surgeon considers there is definite risk of malignancy developing.

Hypnosis in the Treatment of Hyperemesis Gravidarum

THERE has for long been a strong school of thought that contended that there is a definite psychic factor in the etiology of hyperemesis gravidarum. Working upon this hypothesis, W. S. Kroger and S. T. De Lee (*American Journal of Obstetrics and Gynecology*, April 1946, **51**, 544) record successful results from the use of hypnosis in nineteen out of twenty-one patients with this condition. In seventeen instances they used hypnosis alone, whilst in four they used hypno-analysis. The two failures were among those treated by hypnosis. All their patients had previously failed to respond to the more usual forms of treatment, such as dietetic restrictions, sedatives, and parenteral fluids. Full details are given of the method whereby hypnosis was produced. In an experience comprising several thousand cases of hypnosis, the authors claim an incidence of success of about 90 per cent., and they are of the opinion that the technique "can easily be acquired by any physician". It is in the state of complete post-hypnotic amnesia that the suggestion is made to the patient that she will stop vomiting. In five cases one treatment only was required; in the remainder two to six treatments were necessary. In hypno-analysis, which is a rapid form of psychoanalysis under hypnosis, an attempt is made to discover the psychological reasons why vomiting has occurred. In the four patients reported in this series three to five sessions were required to elicit the factors responsible for the vomiting, but in all four vomiting ceased following treatment. No guide is given as to which cases were considered suitable for hypnosis alone and which should be treated by hypno-analysis.

The Treatment of Scarlet Fever with Penicillin

WITH the object of determining the minimal effective dosage of penicillin in the treatment of scarlet fever and also that necessary for the elimination of the carrier phase, a group of 118 patients with scarlet fever were observed at the U.S. Naval Hospital, Treasure Island, California, during the period of February to June, 1945 (*American Journal of the Medical Sciences*, April 1946, **211**, 417). Three schedules of dosage were employed:—(1) Total dosage 240,000 units: 10,000 units three-hourly, or 80,000 units per day, for three days. (2) Total dosage 360,000 units: 10,000 units three-hourly or 80,000 units per day, for three days; then 10,000 units six-hourly, or 40,000 units daily for three days. (3) Total dosage 480,000 units: 10,000 units three-hourly or 80,000 units per day for four days, then 10,000 units six-hourly or 40,000 units daily for four days. All the patients were Navy personnel, young and in good health apart from the scarlet fever, diagnosis of which was based upon clinical evidence of pharyngitis, fever and typical rash; in 76 per cent. the initial throat culture was positive for beta hæmolytic streptococci. Throat cultures were taken on the day of admission and every two to three days during hospitalization. All the patients showed good clinical response to

the penicillin therapy, the temperature dropped to normal and there was marked symptomatic improvement within twenty-four to forty-eight hours. All but one patient had negative throat cultures during the course of the penicillin therapy, nor did complications develop in any case during the therapy. Any rise in temperature after completion of therapy, accompanied by rhinitis, otitis media, sinusitis or adenitis, was considered a complication; the incidence of complications after cessation of penicillin therapy was 31 per cent. in the group receiving a total dosage of 240,000 units, 14 per cent. in the group receiving a total dosage of 360,000 units and 6 per cent. in the 480,000 unit group. Also the rate of recurrence of positive throat cultures was highest in the 240,000 unit group (77 per cent.) and lowest in the 480,000 unit group (8 per cent.). From the results obtained it is concluded that a total dosage of 480,000 units of penicillin over an eight-day period is the most effective method for the treatment of scarlet fever and also for the prevention of the carrier state in convalescent patients.

Physostigmine in the Treatment of Rheumatoid Arthritis

MUCH of the pain and discomfort in rheumatoid arthritis are due to the associated muscle spasm. This spasm may persist even when the joint process is inactive and it plays an important rôle in the production of deformities. As a result of their experience in 153 cases, A. Cohen, P. Trommer, and J. Goldman (*Journal of the American Medical Association*, February 2, 1946, 130, 265) recommend the use of physostigmine salicylate for the relief of this spasm. By this means patients are rendered more comfortable and more active, and the tendency to deformities is diminished. In order to eliminate the unpleasant parasympathetic side-effects of the drug, atropine sulphate was given simultaneously with the physostigmine. The initial dose of physostigmine salicylate was 0.6 mgm. (1/100 grain) given subcutaneously along with the same amount of atropine sulphate. If no relief was obtained with this dose, it was raised to 1.2 mgm. (1/50 grain). The dose of atropine sulphate was adjusted in each case according to whether it produced any unpleasant effects, such as dryness of the mouth or disturbance of vision. In successful cases relief was obtained within three to fifteen minutes, and this effect might persist for several days. In some cases, especially when treatment was first begun, the injection had to be repeated daily for a varying period. All the cases treated were of more than six months' duration, and successful results were obtained in 120 of them. In addition, the treatment proved of value in cases of fibrositis and spondylitis.

Treatment of Gastro-Duodenal Ulcer Pain

A NEW method for the treatment of the pain of gastric and duodenal ulcers is outlined by L. Rouguès (*Presse Médicale*, May 11, 1946, 54, 314), who records the results obtained by its use in a series of forty cases. The method consists in the daily administration by mouth of 100 c.cm. of a fresh solution of 1 per cent. novocain, taken in sips on wakening in the morning. The patient lies in the moderate dorsal Trendelenburg position, then right lateral for gastric ulcers and frankly lateral for duodenal. The total absorption of the solution must be completed in twenty minutes and the decubitus must be maintained for one hour. In some cases the dosage was divided into two equal parts and given in the morning and evening. Of the forty cases treated the pain was ameliorated in all except one; in most cases there was marked amelioration after the second or third day; a slight exacerbation may occur during the first two days, after which the crises yield rapidly to the treatment. Recent evolutive duodenal ulcers respond as well to the treatment as do chronic and recent gastric ulcers. The most striking radiological evidence of amelioration was obtained in the group of gastric ulcers; except in one case the cavities in the lesser curvature showed signs of regression, and in one case X-rays showed the complete disappearance of a large cavity in the lesser curvature one-and-a-half months after treatment. No toxic reactions of any importance occurred in the treated series, but in cases of personal idiosyncrasy caffeine is the antidote for the slight nausea or vertigo which may occur. The action of 1 per cent. novocain solution *per os* in such cases as those treated is indubitable but its exact mode of action and its pharmacology are still a matter for investigation.

Quinine Amblyopia

BASING his observations upon seven cases seen during a period of two years in Egypt, A. Bishay (*British Journal of Ophthalmology*, May, 1946, 30, 281) gives the following account of quinine amblyopia. The ages of his patients ranged from eighteen to fifty years. In only two cases was the amblyopia preceded by large doses of quinine; in the remainder it followed ordinary doses. In all seven patients, however, the onset of blindness was preceded by vomiting and some loss of consciousness. Tinnitus and deafness were not the rule. The principal ophthalmic findings were: (1) anæmic,

blanched conjunctiva; (2) partial anæsthesia of the cornea; (3) dilated pupil; (4) immobile iris; (5) pallor of the optic discs; (6) marked constriction of the retinal blood vessels; (7) marked contraction of the field of vision in those who did not develop complete amblyopia; (8) diminution of colour sense, especially red and green. There are two main theories concerning the cause of this condition—that it is due to a direct toxic action on the retinal cells, and that it is due to anæmia of the retina produced by extreme vasoconstriction of the retinal vessels. Bishay is of the opinion that neither of these factors can account entirely for the condition, and he suggests that a third causative factor must be considered, i.e., sensitiveness of the patient to quinine. The main form of treatment hitherto has been full doses of strychnine, but in the two patients in this series in whom paracentesis was performed at once, followed by the administration of strychnine, better and quicker results were obtained than in those who received strychnine only.

An Investigation of Artificial Sunlight

ALTHOUGH ultra-violet light treatment has been in vogue for many years, there has been little, if any, convincing evidence concerning its efficacy in conditions other than rickets. A carefully controlled investigation sponsored by the Industrial Health Research Board (*Artificial Sunlight Treatment in Industry*. By Dora Colebrook. H.M. Stationery Office, 1946. Price 1s.) suggests that such treatment is of little value in the prevention of "colds" or in the reduction of sickness absence among workers. Three thousand workers were included in the study, drawn from a Government office, a motor factory in the home counties and a coal mine in Durham. The criteria adopted were:— (1) sickness absence in each of the three communities; (2) the duration of colds in the clerical and factory workers; (3) injury and total absence among the miners. In none of these respects was any benefit derived from irradiation with wavelengths shorter than 3,300 A.U., i.e., those wave-lengths in the ultra-violet region which can prevent and cure rickets and are also responsible for producing erythema in the skin. This report is of value, not only on account of its findings, but also because of the detailed account it contains of how such a study should be carried out in order to attain results which are capable of statistical analysis. In the past so many reports on the action of ultra-violet light have been vitiated because of the faulty methods used, that it is to be hoped that in planning future experiments investigators will devote

careful attention to this report. It is a model of its kind.

The Correct Posture in Sleep

ACCORDING to J. McDonnell (*British Journal of Physical Medicine and Industrial Hygiene*, May-April, 1946, 9, 46) there is only one correct sleep posture for the healthy individual: lateral recumbency with secure anchorage of the pelvis. This last is obtained by placing the internal aspect of the uppermost knee in the mattress external to the underlying limb (fig. 1). The
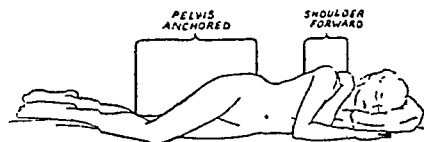
FIG. 1.

degree of flexion of the lower limbs is a matter of individual adjustment. It is also essential to obtain correct alignment of the vertebræ, and this is attained by placing the uppermost elbow on the mattress or as near it as the build of the individual will allow. Adequate support of the head is also necessary, and this is obtained as follows: on lying down in bed the head is maintained in the same position as would be done in the erect position, and the gap between the mattress and the individual's head is then filled by the pillow (fig. 2). Those who sleep on their

FIG. 2.

back are liable to lumbosacral strain unless the thighs are supported in a flexed position, whilst sleeping in the prone position causes rotation of the cervical vertebræ. McDonnell believes that faulty sleep posture is often responsible for intercostal neuralgia produced by strain of the interspinous ligaments following mal-alignment of the vertebræ. He has found that no patient with intercostal neuralgia had adopted the sleep posture he describes, and that conversely no patient who adopted this position has suffered from intercostal neuralgia.

lood Sedimentation Tube Holder

SEDIMENTATION tube holder, designed to enre the vertical position of the tubes and ntrol of the temperature at which the tests e performed, is described by K. B. Rogers *ancet,* April 6, 1946, i, 502). As shown in jure 1, the holder fits over the top of the
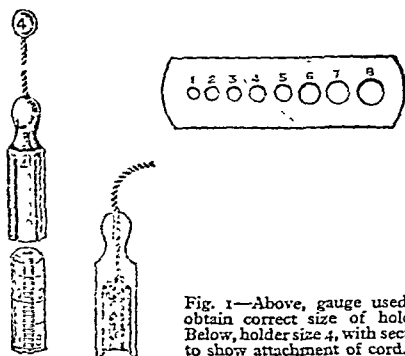
Fig. 1—Above, gauge used to obtain correct size of holder. Below, holder size 4, with section to show attachment of cord.

:dimentation tube and allows it to act as its wn plumb line: the tube is passed through a erforated lid into water at the required temerature, and the water stops the tube swinging iithin a few seconds. The gauge, also shown in igure 1, is used to determine the size of holder to e ordered, i.e., the size of the hole in which the ube fits most closely. Figure 2 shows the tubes a holders suspended in a 7-lb. sweet jar, the ise of which and a standard temperature of 20° ·. are advocated by the author. If the room emperature is 5 per cent. above or below 20° C. he large bulk of water can be cooled or warmed

Fig. 2—Method of using confectionery jar containing water at 20° C. with perforated lid for suspending tubes in holders.

0.5° C. in an hour. The holders, which are manufactured by Willen Bros., Ltd., 44 New Cavendish Street, London, W.1, were originally made for use on the Wintrobe tube, but can be used equally well on the Westergren tube by placing a "policeman" to close the lower end and a false cardboard top to raise the perforated lid on the sweet jar. Rogers has used the holders for over 2,000 tests with the Wintrobe tube and for over 600 with the Westergren, and hopes later to publish details of experiments to show the importance of controlling the temperature, which is made easy by the use of the holders.

Desensitization to Insect Bites

THE results obtained in a series of 129 infants susceptible to flea bites, by inoculation with a flea antigen consisting of an extract of whole fleas of cats, dogs and human beings (*Ctenocephalides felis, Ctenocephalides canis* and *Pulex irritans*) in phenolated, isotonic saline solution, are recorded by A. Hatoff (*Journal of the American Medical Association,* March 30, 1946, **130**, 850). The average age of the patients treated was four years, and the dosage aimed at was 0.1 c.cm. flea antigen initially, and then 0.2 c.cm. for the remainder of a course of at least three inoculations for children up to five years of age, and for those over five years an initial subcutaneous injection of 0.2 c.cm. and then 0.4 c.cm. for at least five injections, given every other day. The average time of response following injection was eight days; 100 children (78 per cent.) were benefited, in 6 the results were transient, and in 23 there was no response to treatment. Incised wheals were observed in 84 per cent. of cases, and in the remaining 16 per cent. no wheal was observed. Secondary infection occurred in 20 cases (16 per cent.), in three in the form of impetigo contagiosa. Irritation and pruritus occurred in all cases. The average number of injections given was four. In his conclusion the author draws attention to the possible value of the method as an adjunct in the control of insect-borne disease.

A Midge Repellent

ACCORDING to a report in *The Pharmaceutical Journal* (April 6, 1946, **156**, 219), a team of biologists working under the auspices of the Scientific Advisory Committee of the Department of Health for Scotland has found dimethylphthalate (D.M.P.) to be the most effective protection against midge bites. D.M.P. is the mosquito-repellent which was used extensively during the 1939-45 war. The most satisfactory results were obtained with the following formula:—

Lanette wax SX	5 gm.
Triethanolamine	9 c.cm.
Oleic acid	27 c.cm.
Dimethylphthalate	100 c.cm.
Water	100 c.cm.

This emulsion is said not to be injurious to the skin, although it may occasionally cause slight tingling of the skin; the only precautions that need to be taken are that it should not be allowed to get into the eyes, nor should it be allowed to come in contact with tortoise-shell or plastic spectacle frames.

REVIEWS OF BOOKS

Injuries and Diseases of the Oesophagus.
By G. GREY TURNER, M.S., F.R.C.S.
London: Cassell & Co., Ltd., 1946.
Pp. 100. Figures 19. Price 15s.

THE only part of this book that can be criticized is the preface. Mr. Grey Turner writes that the Hume lectures, which it presents, are a record of his own experience and are not intended to be a complete account of the subject; yet this book represents one of the best surgical monographs on any subject, certainly the most comprehensive and practical account of the diseases and injuries of the oesophagus in existence, a realm of surgery that he has made his own particular province. The subject is covered with a completeness that is remarkable in less than 100 pages, many of which are occupied by illustrations. Examination and diagnosis, congenital abnormalities, diverticula, foreign bodies, injuries by corrosives, the management of mediastinitis, non-malignant stricture, achalasia, peptic ulcer, non-malignant and malignant tumours, are all dealt with in a practical and helpful manner, for the statements are supported by clinical accounts of cases, and the illustrations all play their part in explaining or expanding the statements in the text. Mr. Grey Turner's style is by now well known, one in which sincerity and erudition are fired by an ever youthful enthusiasm. The practitioner in search of interest and enlightenment and the surgeon in need of detailed instruction will alike turn to this book with pleasure and profit.

Venereal Diseases in General Practice. By
SVEND LOMHOLT, O.B.E., M.D. London:
H. K. Lewis & Co., Ltd., 1946. Pp. 231.
Illustrations 117, with 39 in colour.
Price 25s.

THE author of this work on venereal diseases needs no introduction to British readers, in fact his reputation is world wide. He tackles his subject on conventional lines, a procedure which accords with British principles. In turn, syphilis, chancroid and gonorrhœa are considered at some length, whilst phagedæna, lymphogranuloma inguinale, granuloma venereum, balanoposthitis, herpes genitalis, condyloma acuminatum, molluscum contagiosum, phthirus pubis, and simple (non-specific) urethritis, receive brief mention. It should be noted that the book was written in 1939; an Appendix (1945) is devoted to penicillin, mapharside, intensive methods of treating syphilis, and the newer sulphonamides, thus bringing the treatment up to date. For the

treatment of syphilis the concurrent, intermittent use of arsenic and bismuth is recommended and the value of the latter is rightly stressed. For gonorrhœa the Neisser injection treatment, carried out by the patient himself, is preferred to grand lavage by the Janet method. By far the best part of the book is that on the syphilides, the diagnosis being set out more clearly; the figures are excellent, whilst the coloured plates are beautifully reproduced and could hardly be surpassed. The reader will do well to note the views expressed as to the value of the complement fixation test in gonorrhœa and its complications.

*Cancer of the Scrotum in Relation to
Occupation.* By S. A. HENRY, M.D.,
F.R.C.P., D.P.H. Oxford University Press
(Oxford Medical Publications), 1946.
Pp. viii and 112. Figures 30. Price 15s.

THIS well-illustrated monograph, based upon a Hunterian lecture, provides a detailed study of the incidence of scrotal cancer. No effort has been spared by the author in this painstaking work. He has collected a vast amount of factual evidence and shows the close relationship existing between occupation and this particular form of malignant disease. Such a detailed study would hardly have been possible unless the author had been deeply interested in the subject over many years. An examination of fatal cases brings out the higher incidence of this disease among those exposed to certain coal products and to mineral oil, and analysis of the notification of cases of epitheliomatous ulceration has disclosed the fact that of over 3,000 such notifications over a period of twenty-three years, some 40 per cent. were scrotal, and of these, cotton mule spinners provided 60 per cent. A short section is devoted to prevention and notice is there taken of the progress in the preventive methods adopted in the textile industry. One minor criticism must be added—a book which contains so much valuable material is worthy of something better than a paper cover.

*Rare Diseases and Some Debatable
Subjects.* By F. PARKES WEBER, M.D.,
F.R.C.P. London: Staples Press Ltd.,
1946. Pp. 174. Illustrations 18. Price 15s.

DR. PARKES WEBER occupies a unique position in English medicine as a collector of, and authority on, rare diseases. There can be few medical men in this country who have had more diseases named after them than this connoisseur of the

and the old. In this volume he has collected
:ther some of his more recent articles, and
ıy readers will be glad to have in such con-
:ient form this guide to some of the rareties
ıedicine. The titles of the chapters alone will
late the palate of many a clinician: "Paget's
ıe disease in three sisters", "Congenital
ndice in a man aged 77", "A glycosuric
ıily without hyperglycæmia". The book
ıcludes with some of those "random
ıughts" which the author has periodically
ıtributed to medical thought, e.g., "Boun-
ıus nature and over-nutrition", "Explanation
the urge to collect". There will be few readers
ıo will not "excuse the occasional repetition"
which the author refers in his foreword.

andbook of Infectious Diseases. By THE
STAFF OF THE CANTACUZÈNE INSTITUTE
UNDER THE DIRECTION OF PROFESSORS
C. IONESCU-MIHAESTI AND M. CIUCA.
League of Nations Publications No. 3,
Geneva, 1945. London: Allen & Unwin
Ltd., 1946. Pp. 331. Figures 11, includ-
ing 5 coloured plates. Price 5s.

ʜɪs pocket-sized handbook, which is dedi-
ated to the memory of Professor J. Cant-
cuzène, contains, in addition to notes on
ırophylaxis, serum treatment and vaccination,
ıuch useful information on the routes of
ınfection, incubation periods, symptoms, diag-
ıosis and treatment of infective diseases. The
ɔloured plates included in the chapter on
ɔiological tests are of value for the estimation of
ıhe required reactions. The techniques of
immuno-transfusion, serum treatment, inocu-
lation and vaccination are described in detail in
their respective chapters, and another useful
inclusion is a chapter on the collection of
specimens for diagnosis. The work is a most
welcome contribution to the study, prevention
and treatment of infective diseases and should
have a wide appeal, particularly among those
working in war-devastated areas.

Arbuthnot Lane: His Life and Work. BY
W. E. TANNER, M.S., F.R.C.S. London:
Baillière Tindall & Cox. Ltd., 1946.
Pp. 192. Price 15s.

ᴛʜɪs biography of Lane will be read with
interest by all past and present students of
Guy's Hospital, and by all those who ever
encountered the man who dominated British
surgery for thirty years. Lane, throughout his
life, was an inspiration and an enigma. He had a
commanding presence and an easy charm of
manner, yet his inner personality remained aloof
even to those who had worked with him for

years. He could inspire the most fanatic loyalty
and arouse the bitterest opposition, yet seemed
unconscious of both. He had a disarming way
of announcing his views as self-evident truths
and meeting criticism by ignoring it. He was a
pioneer in every branch of surgery, but never a
careerist. He fought without rancour. He gained
the highest honours but remained to the end
simple and humble. Tanner follows his old
chief through each stage of his career, his
childhood, his student days, his many years on
the staff of Guy's Hospital, his visits to America,
his retirement. He tells of his early contributions
to surgery, many of which were forgotten in the
controversy that raged around his later interests,
the operative treatment of fractures and of
intestinal stasis. He shows that Lane was the
first surgeon to drain the mastoid antrum, to
resect a rib for empyema, that he led the way
in the treatment of cleft palate, and that he was
the real founder of modern orthopædics. The
frontispiece is a reproduction of Newling's
portrait of Lane presented to the Governors of
Guy's Hospital by his former House Surgeons
in 1932. A bibliography of more than 400
publications is appended.

NEW EDITIONS

Disorders of the Blood, by SIR LIONEL WHITBY,
C.V.O., M.C., M.D., F.R.C.P., D.P.H. and C. J. C.
BRITTON, M.D., D.P.H., in its fifth edition (J. &
A. Churchill Ltd., 30s.) has been enlarged by
the addition of sixty-two pages of text and some
new illustrations. In the chapter on hæmag-
glutination and blood transfusion a much
extended section has been devoted to the Rhesus
factor, and a section dealing with tests for its
detection has also been included in the chapter
on technique. The work has been brought up to
date in all sections and the new edition repre-
sents one of the most comprehensive works on
the blood in present-day literature.

A Short Practice of Surgery, by HAMILTON
BAILEY, F.R.C.S., F.I.C.S., and R. J. McNEILL
LOVE, M.S., F.R.C.S., F.I.C.S., in its fifth edition
(H. K. Lewis & Co. Ltd., 40s.) contains an
entirely new chapter on "the larynx", and many
of the chapters have been rewritten in the light
of surgical advances since the appearance of
the previous edition in 1943. The new edition,
as its predecessors, is richly illustrated, con-
taining in all 1,063 illustrations, some of which
are coloured. In the preface the authors quote
the Chinese proverb "one picture is worth a
million words", which maybe was meant to
convey a somewhat different meaning to that
suggested; nevertheless, the illustrations in this
well-known textbook undoubtedly add greatly
to its value without in any way detracting from
the praise due to the written instructions.

NOTES AND PREPARATIONS

NEW PREPARATION

PANTOTHENIC ACID 'ROCHE' (dihydroxy-di-methyl-butyryl-alanine), a colourless, slightly acid substance, soluble in water and alcohol and made available in crystalline salts (calcium, sodium) or as an alcohol ('panthenol'), is a factor of the vitamin B complex. Although the drug is still somewhat in the experimental stage, reports are available of its successful use in the treatment of achromotrichia and alopecia, in affections of the skin, rhinitis, herpes, corneal ulcers and conjunctivitis, and in chronic bronchitis. Deficiency of pantothenic acid is said to affect the epithelial tissues, the respiratory and gastro-intestinal systems, and growth and health generally. Pantothenic acid 'Roche' is issued in 25 mgm. tablets, in bottles of 100, by Roche Products Ltd., Welwyn Garden City, Herts.

AMENDMENTS TO THE BRITISH PHARMACOPŒIA, 1932

A NOTICE issued by the British Pharmacopœia Commission announces the annulment of the amendment to the British Pharmacopœia, 1932 (sixth addendum) concerning the omission of quinine from the formula of Easton's syrup. Another announcement concerns penicillin preparations: Two *B.P. Penicillin Creams* (*Crem. Penicil.* and *Crem Penicil. Sterilisat.*), both containing 50,000 units of penicillin, and one of which is sterilized for use in the treatment of infected lesions, become available on prescription. *Injection of Penicillin B.P.* (*Inj. Penicil.*), when no particular strength is stated on a prescription, will contain 20,000 units of penicillin per c.cm. *Oily Injection of Penicillin B.P.* (*Inj. Penicil. Oleos.*) is made up with a penicillin content of 12,500,000 units (dosage: 1 to 4 c.cm., i.e., 125,000 to 500,000 units). *Penicillin Eye Ointment* (*Oculent. Penicil.*) has a penicillin content of 100,000 units; *Penicillin Lozenges* (*Troch. Penicil.*) 500 units of penicillin per 1 gm. tablet, and *Ointment of Penicillin* (*Ung. Penicil.*) 50,000 units, in an ointment base of Wool Alcohols.

DIPHTHERIA IMMUNIZATION

THE report of the Social Survey Inquiry on Diphtheria Immunization, carried out for the Ministry of Health, has just been issued. Of the 2,000 mothers interviewed 81 per cent. with one or more children over the age of one year had had at least one child immunized, 35 per cent. on their own initiative, 34 per cent. at the suggestion of the school, 19 per cent. at the suggestion of the welfare clinic, and 6 and 5 per cent. at the suggestion of health visitors and medical practitioners respectively. No marked difference between immunized children i towns and rural districts was noted.

VITAMIN CHART 1946

A VITAMIN chart, showing the formulæ of tł different vitamin substances, their commo names, their vitamin potency, dosage and ii dications, has been compiled by the Crook Laboratories, Gorst Road, Park Royal, Londo N.W.10. Copies may be obtained on applicatio

NATIONAL ASSOCIATION FOR TH PREVENTION OF TUBERCULOSIS

THE twelfth edition of the Directory of Di pensaries, Clinics and Sanatoria, entitle *N.A.P.T. Handbook of Tuberculosis Activitie* has been issued by the National Associatio for the Prevention of Tuberculosis. In additio to information concerning activities in Gre Britain the new edition contains particulars c tuberculosis institutions and activities through out the Empire. Copies can be obtained fror the National Association offices, Tavistoc House, Tavistock Square, London, W.C.1. Tw other recent issues by the Association are th *Tuberculosis Index and Abstracts of Curre Literature*, edited by J. H. Harley William M.D., D.P.H., and a new and well-produce magazine *Health Horizon*, published monthly price 1s. 6d. or 5s. per annum.

ROYAL PHOTOGRAPHIC SOCIETY MEDICAL GROUP

A MEDICAL Photography Group of the Asso ciation for Scientific Photography, which ha been amalgamated with the Royal Photographi Society, was formed on April 1. Rear Admir C. P. G. Wakeley, D.Sc., F.R.C.S., was electe Chairman. Those interested can obtain par ticulars from Mr. E. J. Andrews, A.R.P.S Hon. Secretary, Medical Group, but those wh wish for membership should apply to the Hor Secretary, Royal Photographic Society, 1 Princes Gate, London, S.W.7.

E. & S. LIVINGSTONE'S CATALOGUI OF MEDICAL BOOKS

THE new illustrated catalogue (April 1946 issued by E. & S. Livingstone Ltd. (16-1 Teviot Place, Edinburgh, 1), entitled "Medica Books, April 1946", is a fine example of wha publishers' catalogues should be. It is beauti fully illustrated, clearly printed, and a pleasur to read. Copies are available on application.

THE MALARIA PATIENT

By BRIAN MAEGRAITH, M.B., D.Phil.

Professor of Tropical Medicine, School of Tropical Medicine, University of Liverpool.

MALARIA must be considered as a possible cause of any febrile illness occurring in persons who have been exposed to the risk of infection. At present, when ex-service men and women and repatriated internees are scattered over the whole country, the diagnosis of malaria is particularly important, and the practitioner may be called upon at any time to make it. The following article has been written with the object of helping him to do so.

An attack of malaria may be either a primary attack or a relapse. A primary attack usually develops after an incubation period of ten to fourteen days and is most frequently seen in England in individuals, e.g. seamen, who have recently been exposed to infection in malarial areas, such as those of West Africa. The incubation period may be much longer, sometimes as long as eight or nine months. Delayed primary attacks of this sort are common in benign tertian malaria and are frequently met in servicemen who have been infected in the Italian, Indian and Burmese theatres of war.

Malaria appears in this country, however, most often in the form of relapses of benign and malignant tertian. A relapse is a recurrence, subsequent to recovery from the initial attack, of the symptom complex of malaria and the appearance of parasites in the peripheral blood. Relapses must be distinguished from reinfections; a recrudescence of malaria can be called a relapse only if the patient is at the time away from the endemic area. Relapses often appear a few weeks after the stoppage of suppressive treatment and are liable to occur at fairly regular intervals of weeks or months thereafter, the length of the interval being determined to some extent by the strain of the infecting parasite. Such relapses may continue over a period of years, but it is unusual for malaria of any kind to continue relapsing after the patient has been more than three years out of the endemic area.

CLINICAL FEATURES

In all forms of malaria, relapses and reinfections follow much the same course as the primary attack. However, attacks vary in severity and risk to the patient according to the species of the invading plasmodium. In general, benign tertian, quartan and ovale malaria do not offer serious hazards to the life of the individual, although the clinical features of the attack are often

severe, unpleasant and sometimes frightening. Malignant tertian, on th other hand, is always potentially dangerous, although the clinical manifest: tions in the early stages and in the chronic low-grade forms of the disea: may not seem severe.

For all practical purposes, only benign tertian and malignant tertia malaria need be considered here. Quartan and ovale malaria behave in th main like benign tertian.

BENIGN TERTIAN MALARIA

The classical attack is cyclical, the cycle of paroxysms being related to th phases of development of the invading plasmodia. In the established cas the paroxysms occur at regular intervals, which are usually quotidian (th paroxysms appearing daily) or tertian (the paroxysms appearing every thir day), with intervening apyrexial periods. This regularity is not always see in the first few days of the primary attack, during which the pyrexia is ofte irregular and may be continuous or remittent. In the relapse the paroxysm may be modified in severity, but are otherwise indistinguishable from thos of the initial attack; the periodicity in the relapse is usually the same as tha of the primary attack.

Prodromal symptoms.—For some days before the onset of an attack th patient may complain of headache, pains in the limbs and back (not unlik those of influenza), lassitude, anorexia and frequently of "shivering feelings" Sometimes there may be nausea and vomiting. Occasionally the attack ma' appear suddenly without any prodromal symptoms, but this is unusual.

The paroxysm.—The characteristic paroxysms of benign tertian malari: progress in three well-defined stages.

The first, the *cold stage*, begins abruptly. The patient feels chilly and starts to shiver, frequently passing into a violent rigor, with chattering teeth. He complains of bitter cold and covers himself with bedclothes coats and any available covering in his attempts to keep warm. Anorexia nausea and vomiting are common and may be so severe as to suggest food poisoning. The patient looks slightly cyanotic with cold skin and small, fast pulse. There is commonly frequency and polyuria. The temperature rises rapidly to 104° F. (40° C.) or more at the height of the rigor.

The cold phase lasts about a quarter of an hour and is followed directly by the *hot stage*. The rigor ceases and the patient feels progressively hotter. In his effort to get cool he often throws off the clothes so carefully gathered in the cold stage. He complains of thirst and frequently of pains and aches all over the body, particularly in the head behind the eyes. He is restless and excited and may pass into a state of delirium. Nausea and vomiting are common. The skin is hot and dry, the face flushed, the pulse fast and full. The temperature remains what it was at the end of the cold stage, i.e., usually 104° F. to 105° F. (40° C. to 40.6° C.) or may rise.

After an hour or two the *sweating stage* starts. The sweating appears first on the forehead and face and spreads rapidly over the whole body. In most

cases it becomes profuse, the sweat literally pouring off the body and soaking pyjamas and bedclothes alike. The temperature and pulse rate fall rapidly and the subjective symptoms are quickly relieved. Sweating may last for as long as three hours, at the end of which the patient frequently falls into an exhausted sleep, from which he awakens considerably refreshed.

The *apyrexial stage* follows the paroxysm. During this interval the temperature may occasionally rise to as much as 101° F. (38.3° C.), but it is usually normal or below and remains at about this level until the next paroxysm. The patient feels well and, when the periodicity of the attack is tertian, frequently refers to the interval as "my good day".

Without treatment, the above picture of paroxysms at regular intervals will go on repeating itself for weeks and occasionally for months. The cycle of paroxysms is self-limited, however, and will eventually end in apparent clinical cure. After a period of quiescence, the length of which is determined in part by the strain of the invading plasmodium, the cycle is repeated and the disease relapses. The clinical features of the relapse, as has been said above, are indistinguishable from those of the established initial attack. The total length of the attack, measured in terms of the number of paroxysms developed, is, however, usually shorter in the relapse than in the primary attack.

Serious *complications of paroxysms* are few in benign tertian malaria. Bronchitis is not uncommon and pneumonia may occasionally appear. Herpes febrilis is present in about one-third of all cases, appearing usually on the lips, but sometimes also on the nose and pinna of the ear.

The spleen is palpable in most cases. It is rarely felt more than one or two fingers' breadth below the costal margin, except in long-standing cases, but during the paroxysm it may become further enlarged and tender, causing the patient considerable abdominal discomfort.

In benign tertian malaria the degree of anæmia present is seldom severe. The red cell count is not usually less than 3.5 to 4 million per c.mm. The blood picture is that of a mild macrocytic hyperchromic anæmia; there are no characteristic changes in leucocytes.

MALIGNANT TERTIAN MALARIA

It has been pointed out that in the early stages of the primary attack of benign tertian malaria the pyrexia is often irregular and that when the disease becomes established paroxysms usually occur regularly. Sometimes no such regularity develops. Irregular fever in malaria probably indicates the presence of several groups of parasites sporulating at different times. In benign tertian, quartan and ovale malaria, all groups of parasites tend to fall into step, but in malignant tertian malaria this is not the case and a regular series of paroxysms is the exception rather than the rule. In general, in malignant tertian the cold stage of the paroxysm may be short or absent and the hot stage prolonged; the sweating stage may be absent and the apyrexial interval shortened or absent.

Malignant tertian malaria may occur as a short sharp acute attack or it may drag on for weeks or months. It may fulminate at any stage.

The *prodromal symptoms* may last only a few days but sometimes persist for weeks before an overt attack of malaria develops. The patient complains chiefly of malaise, shivering feelings, headache and backache, the latter being usually low down in the lumbar or sacro-iliac region. He is off his food, nauseated, and may sometimes vomit. He is usually miserable and depressed and inefficient in his day's work. If he has had malaria before he will often recognize the symptoms, but too much reliance must not be placed upon this, since most malarious patients tend to blame the disease for all their physical ills.

The attack.—The onset of malignant tertian malaria may be sudden but is more often insidious. Rigors at the onset are uncommon. The fever may be periodic or continuous, with regular periodic exacerbations. It may be remittent or intermittent. There are sometimes double peaks in the temperature chart resembling those seen in kala-azar. In mild attacks, the fever may be low grade and show no periodic features. In some cases, even when the degree of parasitæmia is high, there may be no fever at all. Sweating occurs irregularly. Anorexia, nausea and vomiting are common in severe cases. The appearance of the patient during the attack depends to a large extent upon the development or otherwise of complications. In the uncomplicated case the face is usually flushed, the skin hot and slightly moist and the pulse fast and bounding. The patient may be dull and apathetic or restless, irritable and excited. Backache and headache are almost invariably present. Nausea and vomiting are common. Herpes labialis occurs in about one-third of cases. When there is no fever the patient may present with practically no signs or symptoms beyond a vague feeling of illness and possibly of backache and headache. In pernicious attacks the picture is complicated and often resembles that of other conditions (see p. 85).

The spleen is palpable in most established cases and in long-standing infections it may become very large. Such splenomegaly is unlikely to be seen in patients in this country, except occasionally in children who have been exposed to infection for prolonged periods. During the acute attack the spleen often increases in size, probably as the result of congestion and, as in other forms of malaria, may give rise to dragging pain and abdominal discomfort, sometimes referred to the left shoulder region.

In malaria, anæmia naturally follows the break-up of normal and parasitized red cells. The degree of anæmia depends upon the duration of the disease and the degree of the malarial invasion of the cells. This latter is much greater in malignant tertian than in other forms of malaria, so that patients suffering from this disease are liable to develop very severe anæmia. Red cell counts of 2 to 3 million cells or even fewer per c.mm. are commonly met with, even in the course of the primary attack, and in the chronic infection and after repeated reinfection, polychromasia, basophilia, poikilocytosis and anisocytosis may be found. In severe cases nucleated red cells

may also appear in the peripheral blood; very rarely megaloblasts may be present. In such circumstances the picture may closely resemble that of pernicious anæmia, but the bone marrow reaction in malaria is almost always predominantly normoblastic. Enlargement of the liver associated with epigastric pain and discomfort and sometimes bilious vomiting and jaundice, is not uncommon in severe malignant tertian malaria.

Enough has been said above to indicate that malignant tertian malaria without complications may present no very characteristic clinical features. The important thing to realize is that *serious complications may develop at any stage of the disease, from the onset to the relapse.* Some space must therefore be given to discussion of the clinical features of such complications.

PERNICIOUS ATTACKS

Severe complications of malaria are usually referred to as pernicious attacks. In the vast majority of cases such attacks result from malignant tertian infection, but occasionally they may complicate the other forms of malaria. Pernicious attacks may develop suddenly at any stage of the disease, both in apparently mild and obviously severe cases. The commoner clinical types of pernicious malaria may be roughly grouped as follows: (1) hyperpyrexial, (2) cerebral, (3) gastro-intestinal, (4) algid forms and (5) blackwater fever.

HYPERPYREXIA.—This may develop during an ordinary malignant tertian attack or it may appear as an early sign without accompanying evidence of malaria and so be mistaken for heat hyperpyrexia. It is sometimes associated with the cerebral form of malaria. The temperature rises rapidly to 107° F. (41.7° C.) or higher in the course of a few hours. In some cases the rise of temperature is uncontrollable, but usually the pyrexia can be controlled by appropriate methods, such as tepid sponging. By the time he is seen by the doctor the patient is often in delirium and may sometimes be maniacal. He is dyspnœic; the skin is hot and dry and there may be some cyanosis. The erythrocytes are usually heavily invaded by plasmodia. In untreated cases coma supervenes.

CEREBRAL MALARIA.—Cerebral complications may develop at the onset of the first attack of malaria, but are commoner after long-continued low-grade infections. The onset is sometimes sudden but more often gradual, the signs and symptoms developing over a period of days. Frequently the first thing noticed is unusual behaviour on the part of the patient, often put down to alcohol. The patient complains of headache, and often of drowsiness and, if untreated, rapidly passes into a coma. In this state the face is suffused, the pupils contracted, and the knee-jerks exaggerated. There is often stiffness of the neck and, in the more advanced stages, muscular twitchings and convulsions. The temperature is usually high and may go on to hyperpyrexia. Sometimes the condition ends in a state of convulsions, resembling those of epilepsy. This so-called epileptiform type of cerebral malaria is usually associated with acute psychical disturbances, in the early stages of which the patient may be violent. Other forms of

cerebral malaria are sometimes referred to as encephalitic, meningeal and paretic. Frequently the clinical picture is the mixed one. Parasites may be scanty in the peripheral blood, or there may be a massive infection.

GASTRO-INTESTINAL COMPLICATIONS OF MALARIA

(a) *Bilious remittent fever.*—The patient suffers from gastro-intestinal disturbances from the onset. He complains of nausea and begins vomiting early in the disease. The vomiting may become insistent, and not infrequently the vomitus is coffee grounds and sometimes contains frank blood; it usually contains bile. As the disease progresses the patient suffers from all the consequences of persistent vomiting. Diarrhœa is a frequent and early symptom. The liver becomes enlarged and tender, and there is pronouced icterus which usually appears about the second day. The patient frequently passes into a typhoid state with characteristic remittent fever.

(b) *Dysenteric form.*—This form of pernicious malaria is characterized by the passage of blood and mucus at frequent intervals. Examination of the stool shows blood, mucus, and epithelial and cellular debris. When the condition has gone on for more than twenty-four hours there may also be pus. There is often nausea and vomiting. The temperature is frequently high and remittent. The disease may be clinically indistinguishable from acute bacillary dysentery, which may occur contemporaneously and must be excluded.

(c) *Choleraic form.*—The patient suffers from profuse watery diarrhœa and may become extremely dehydrated. There is usually associated nausea and vomiting and, commonly, severe abdominal cramps. The stool is mainly fluid containing particles of fæces, sometimes mixed with small amounts of blood and mucus. Suppression of urine and peripheral vascular failure may occur as in true cholera.

(d) Acute pernicious malaria may sometimes give rise to symptoms closely resembling those of acute surgical conditions, such as appendicitis and peritonitis.

ALGID FORMS.—In this condition the patient passes rapidly into a state resembling shock. He is pale, anxious-looking and collapsed; the breathing is shallow, the pulse thin and fast; the skin is cold and covered with clammy perspiration. Although the skin feels cold, the axillary and rectal temperatures are often high, e.g. 103° F. or 104°F. (39.4° C. or 40° C.). The blood pressure is low. This condition of collapse may be associated with choleraic diarrhœa. Parasites are usually present in large numbers in the peripheral blood.

Parasitæmia without clinical signs.—This is one of the most dangerous forms of malignant tertian malaria and may easily be missed. The blood cell infection may be as heavy as 30 to 50 per cent. without any obvious clinical signs, even of fever. Patients with such parasitæmia are in great danger of fatal complications.

BLACKWATER FEVER.—Blackwater fever is characterized by the passage of hæmoglobin and associated pigments in the urine following

severe hæmolysis. The hæmoglobinuria is usually associated with a rise in temperature, but this is not always the case. The disease commonly starts with a severe rigor, either during an acute attack of malignant tertian malaria or in an individual who is suffering from continuous malarial infection. Hæmoglobin may appear in the urine in several waves during the disease, with intervals during which the urine is free from pigments. Jaundice is common and occurs early. There is nausea and vomiting, the patient is anxious and restless, the pulse weak, soft and rapid. Death in untreated cases occurs either from cardiovascular or renal failure. During the hæmoglobinuria the urine contains blood pigments, albumin, casts and debris. Plasmodia are found in the peripheral blood in about 50 per cent. of cases.

THE DIAGNOSIS OF MALARIA

The only way in which malaria can be diagnosed for certain is by the identification of the parasite. In the ordinary course of events the plasmodia will be found as a result of examination of the peripheral blood, but occasionally it may be necessary also to examine the bone marrow. Thick blood films stained by Field's method or by Giemsa's stain should be examined repeatedly in every suspected case. A single negative blood examination does not exclude a diagnosis of malaria. The degree of parasitæmia cannot be gauged by the clinical condition of the patient, severe complications sometimes developing when there are few parasites to be found in the peripheral blood. Study of thin blood films stained by Giemsa's or Leishman's stain is necessary for the certain identification of the invading plasmodium, but examination of the thick blood film is usually sufficient to distinguish between malignant and benign tertian malaria. In the former, except in pernicious attacks, the only stages of parasite seen in the peripheral blood are usually the ring forms and the crescent-shaped gametocytes; in the latter, all stages of the development of the parasite will be seen during the period between one paroxysm and the next.

When a diagnosis of malaria is likely and blood films are persistently negative, injection of adrenaline may occasionally cause parasites to appear. The same effect is sometimes produced by an injection, or a series of daily injections, of crude liver extract, such as hepatex.

The blood picture in malaria, so far as the erythrocytes are concerned, has been referred to already. There are no pathognomonic changes in the white cells. There is sometimes a leucopenia with an increase in monocytes, but this is by no means invariable. The presence of malarial pigment in monocytes and occasionally in polymorphs is, however, significant and can be taken to indicate that the patient is suffering from, or has very recently suffered from, malaria.

It is wise to suspect malaria in all cases of fever occurring in patients who have recently been in endemic areas, but so far as possible a clinical diagnosis of malaria should be avoided. If facilities for blood examination are not immediately available, blood smears should nevertheless be made and examined

at the earliest opportunity. Clinically, the periodic fever of benign tertian malaria is easy to differentiate, but malaria, especially malignant tertian, may simulate many other diseases and complicate other conditions, so that the confirmation of the diagnosis by examination of a blood film must not be taken to rule out other diseases.

The presence of herpes labialis associated with periodic fever is strong presumptive evidence of malaria, as is the combination of anæmia, jaundice and an enlarged spleen. Conditions such as kala-azar in which the spleen and liver are enlarged must always be considered, even after malaria parasites have been found.

When blood examination is impossible a *therapeutic trial test* may be attempted. If adequate doses of quinine or mepacrine do not reduce the fever in three to five days after the institution of treatment, the condition is unlikely to be malaria and the diagnosis must be reconsidered, provided there is no reasonable doubt that the antimalarial drug is being absorbed by the patient. In any serious case, when malaria is suspected, it is reasonable to start treatment before the diagnosis is confirmed.

The clinical diagnosis of malaria *in children* is difficult. Attacks, even of benign tertian malaria, are rarely typical. All grades of fever may be met. Convulsions are common in babies; older children are frequently listless and complain of weariness and headache. There may be relatively gross splenic enlargement. Children are especially likely to develop pernicious forms of malaria. Benign tertian and quartan malaria may be fatal in children, and chronic malaria renders them more susceptible to intercurrent infection, such as pneumonia.

PROGNOSIS

Prognosis in malaria, except in the pernicious forms, is good provided the disease is diagnosed early and adequately treated. Death may occur, however, in pernicious attacks and in cases in which the diagnosis has been missed. With the facilities available in England, this last calamity should never occur if the practitioner is aware of the possibility of the diagnosis.

Malignant tertian malaria will not relapse if the acute attack is adequately treated with either mepacrine or paludrine. Relapses may occur after quinine treatment. Relapses of benign tertian malaria are likely after all forms of treatment. The chance of relapse, however, is least after treatment with a combined quinine and pamaquin course. The relapse can be held off indefinitely by weekly doses of 100 mgm. paludrine, but it is not yet known whether such treatment will eliminate the infection. In between relapses and when taking weekly doses of paludrine, the patient should be quite capable of doing his ordinary work.

TREATMENT OF MALARIA

The patient must be treated in bed, at least until the fever has subsided. When pamaquin is used he must remain in bed throughout treatment. In benign tertian malaria *during the paroxysm* he will probably go to bed only

too willingly, but in low-grade malignant tertian the patient tends to lie about or attempts to go on with his work, and may be difficult to manage. Firmness is important here, owing to the ever present risk of pernicious complications. In well-developed pernicious attacks hospital treatment may be essential, otherwise the patient should be moved as little as possible

CHEMOTHERAPY.—The specific treatment with antimalarial drugs should be instituted immediately the diagnosis has been made. Whenever possible, drugs should be given by mouth. Parenteral administration is, however, indicated in special circumstances, such as intractable vomiting, cardiovascular collapse (as in algid malaria), coma, hyperpyrexia and hyperparasitæmia.

Quinine, mepacrine and pamaquin have been commonly used for years in the treatment of malaria. Recently a fourth drug, paludrine, has been discovered which is in some ways superior to its predecessors. Quinine, mepacrine and paludrine will all effect a cure in the acute malarial attack, whether primary or relapse, either when given alone or in combination with one another. Pamaquin is not used by itself but is invariably prescribed in combination with the other drugs. It can be given concurrently with quinine or paludrine, but it is customary not to give it with mepacrine. Many variations in dosage and combinations of drugs have been recommended for the treatment of malaria but it is pointless to quote more than a few here.

Treatment of the uncomplicated acute attack.—Any of the following courses of treatment will prove successful :—

(a) Quinine, 10 grains (0.65 gm.), t.d.s. for two days.
  Quinine, 10 grains (0.65 gm.), b.i.d. for the succeeding five days.
The quinine is given either as a solution of the bisulphate or as tablets of the hydrochloride or bihydrochloride. Alkali solution may be given immediately after the quinine, but should not be mixed with it. Mixing the two solutions will precipitate the alkaloid. Dose: sodium bicarbonate and sodium citrate., 30 grains (2 gm.) of each; water to 2 ounces (57 c.cm.). Two ounces (57 c.cm.) to be given t.d.s. after quinine for the first two days and then twice daily.

(b) Mepacrine, 300 mgm., t.d.s. for one or two days.
  Mepacrine, 200 mgm., t.d.s. for next day.
  Mepacrine, 100 mgm., t.d.s. for the succeeding five days.
Mepacrine is given as tablets of the hydrochloride, each tablet containing 100 mgm. A draught of water should always accompany the dose.

(c) Quinine, 10 grains (0.65 gm.), t.d.s. for three days.
  Mepacrine, 100 mgm., t.d.s. for five days.
  Interval of two days.
  Pamaquin, 10 mgm., t.d.s. for three days.

(d) Paludrine, 100 mgm., b.i.d. for fourteen days.
Paludrine is given as tablets of the hydrochloride. Water should accompany the dose. The optimal dosage has not yet been worked out; it is probably less than the above.

Treatment of the relapse.—Any of the above courses of therapy will effect clinical cure of the acute attack in all forms of malaria, but in benign tertian the likelihood of further relapses is considerable after such treatment. Experience during the war has shown that the relapse rate can be reduced by the following regime:—

Quinine, 10 grains (0.65 gm.), t.d.s. for ten days.

Pamaquin, 10 mgm., t.d.s. for ten days.

The drugs are given concurrently, so that the full course takes ten days.

In benign tertian infection this combination of drugs, which was first introduced by Sinton, has proved the most successful in reducing the relapse rate, which, following this treatment, is about 10 per cent.; after mepacrine treatment the rate is over 30 per cent.

The effect of paludrine treatment on the relapse rate in benign tertian malaria is still being studied. The present practice is as follows:—On confirmation of the diagnosis a single dose of 300 mgm. is given. This is followed by a dose of 100 mgm. given once weekly for the next six months. So long as the weekly dose is maintained, relapses do not occur. It is not yet known what happens after the drug is discontinued.

Relapses of malignant tertian malaria should be treated with a full course of mepacrine or paludrine, as for the acute attack. Both drugs in adequate amounts apparently sterilize the infection.

Parenteral administration of drugs.—In complicated cases parenteral administration may be essential. The choice of drug at present lies between quinine and mepacrine. Pamaquin is only given orally. Experimental work with paludrine indicates, however, that this drug can be given parenterally with good effect.

Quinine is probably the best drug to use and may be given either intravenously or intramuscularly, in doses of 7½ to 15 grains (0.5 gm. to 1 gm.). This dosage can be repeated twelve-hourly for three or four doses, but the aim of the physician should be to establish oral therapy as quickly as possible.

Intramuscular injection of quinine is painful. The drug damages muscle tissue and may cause necrosis and abscesses unless the injection is given under strict aseptic conditions. Intravenous quinine must be given very slowly, with full aseptic precautions. The solution should be well diluted before injection. If reasonable care is taken with the technique and speed of the injection, there are no unusual risks in giving intravenous quinine therapy. Mepacrine can be given intramuscularly but not intravenously, in doses of 300 mgm. atebrin (mepacrine) "musonate". The injection should be given with the same aseptic precautions as with quinine. The dose may be repeated at twelve-hourly intervals for three or four doses.

TREATMENT OF MALARIA IN CHILDREN

Children take antimalarial drugs well. The dose of quinine is usually calculated on the basis of one twentieth of the adult dose multiplied by the age of the child in years. For example, if the adult dose is reckoned at 30

grains (2 gm.) in the day, then the dose for a child aged four is 6 grains (0.4 gm.). Mepacrine may also be used without fear of complications. Up to the age of two years the child should not be given more than 100 to 150 mgm. in twenty-four hours, but the dose can be increased slowly to 300 mgm. in twenty-four hours at the age of ten. A child of fifteen can be given the full adult dose. Pamaquin should not be given to children. The dosage of paludrine for children is not yet known, but it is likely that they will be able to tolerate large doses of this drug.

THE TOXICITY OF THE ANTIMALARIAL DRUGS

In therapeutic doses *quinine* often gives rise to nausea and some dizziness and tinnitus. These effects are not often severe, but they may be present even on suppressive dosages. Skin reactions due to sensitivity to the drug may occur occasionally. In larger doses quinine may give rise to abortion, but this is not likely on ordinary therapeutic regimes. Very large doses may cause permanent blindness.

In high doses, e.g. 1 gm. or more at a single dose, *mepacrine* causes gastro-intestinal discomfort and vomiting, and sometimes diarrhœa. In therapeutic doses it is not toxic except in rare cases in which it is believed to cause the so-called "mepacrine psychosis". In suppressive doses of 100 mgm. daily, mepacrine has no side-effects, except in a few individuals after the first few doses, when it may give rise to slight abdominal discomfort and diarrhœa. It can be taken continuously in doses of 100 mgm. daily over very long periods without ill-effects.

With *pamaquin* there is little margin of safety between the therapeutic and the toxic dosage. Pamaquin affects hæmoglobin and may give rise to cyanosis of the extremities and lips. In therapeutic doses it sometimes causes acute colicky abdominal pain. The drug is excreted in the urine and may give rise to renal obstruction. Acute hæmolysis followed by hæmoglobinuria may occur during pamaquin therapy, producing a picture indistinguishable from that of blackwater fever. It is therefore necessary to keep the patient in bed during pamaquin therapy. The drug must be stopped at the first sign of toxicity.

One of the great virtues of *paludrine* is its low toxicity. There is a tremendous margin of safety between its therapeutic and toxic doses. Therapeutic activity is found between 10 and 1500 mgm. daily; toxic symptoms appear only at the highest dosages. There is occasional nausea and vomiting at doses of 500 to 750 mgm. twice daily, but no symptoms of sufficient gravity to indicate the stoppage of treatment have been reported over the whole therapeutic range.

GENERAL MEASURES IN THE TREATMENT OF MALARIA

Headache in the acute attack is usually relieved only by clinical cure of the malaria. Because of their supposed slight antimalarial activity aspirin and other anodynes are not usually recommended. Post-malarial headache, however, which is a common complaint, may respond to treatment with aspirin

and similar drugs. Persistent headache of this type may be successfully relieved with doses of nicotinic acid.

In the cold stage of an attack of benign tertian, extra bed coverings and hot-water bottles should be used freely. In the hot stage and in hyperpyrexial attacks, sponging with tepid water or water and vinegar is necessary. In hyperpyrexial pernicious attacks, the temperature should not be brought down below 102° F. (38.9° C.) in the first instance, otherwise the patient may collapse. Pyjamas and bedclothes may need frequent changing in the sweating stage.

Restlessness, delirium and severe intractable vomiting can be treated with barbiturates. Morphine can be given in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain (16 to 32 mgm.) if necessary.

Alkali is said to be useful in cases in which renal failure is threatened, but not more than the equivalent of 15 to 20 gm. of sodium bicarbonate should be given in twenty-four hours. It is usually prescribed to promote diuresis and, provided the kidneys are functioning efficiently, may do so. When renal function is disturbed, as in blackwater fever, alkali must be used with caution.

Fluid and sodium chloride.—It may be necessary in severe cases to replace fluid and salt lost by sweating, vomiting or choleraic diarrhœa. The patient should always be encouraged to drink freely and intravenous drip infusions may be given as required. A check must be kept on the daily intake of fluid. It is very easy and very foolish to overload and waterlog a patient with fluid, especially in anuria, with consequent serious embarrassment of the cardiovascular system.

Fluid and salt are replaced usually by the intravenous injection of physiologically balanced saline solutions, to which may be added 5 per cent. glucose. Quinine may be added to the infusion. The amount of fluid given in a case must be decided by clinical observation and the relation of intake of fluid to output.

Blood transfusion may be essential in severe cases of malignant tertian in which hæmolysis is rapid or destruction has continued for some time. Hæmolysis reduces the oxygen carrying power of the blood, and the only way to restore this is to replace the lost red corpuscles. The point at which transfusion becomes necessary will have to be decided on clinical grounds, but a good working rule is that if there are fewer than 1.5 million corpuscles per c.mm. transfusion is advisable. The fluid given with the transfusion must be calculated in estimating the fluid intake.

Autoagglutination is common in malaria and the agglutinins of the plasma are often increased. It is therefore necessary before transfusion to *cross-match the donor's corpuscles with the patient's serum* and *vice versa:* grouping is not itself sufficient. In blackwater fever some of the donor's cells may be lysed, but this is not a contraindication to transfusion.

Anæmia.—Malarial anæmia should be treated on general lines, with the administration of iron, liver extracts and vitamins when necessary. In resistant cases a single blood transfusion may be useful.

AMŒBIASIS

By Lieut.-Colonel W. H. HARGREAVES, O.B.E., M.R.C.P.

From The Queen Alexandra Military Hospital, Horley, Surrey.

Amœbic infection is one of the aftermaths of war which will face practitioners in Britain for some years to come, as millions of troops have been serving in areas where amœbic dysentery is endemic. In the South East Asia Command the problem of diarrhœa and dysentery was second only to that of malaria (Marriott, 1945), amœbæ being found in 20 per cent. of such cases, and in Eastern India amœbic dysentery was one-and-a-half times as common as bacillary dysentery (Payne, 1945). As the result of the use of mepacrine and the sulphonamides, malaria and bacillary dysentery have now ceased to be war problems, but amœbic dysentery is still a serious cause of invalidism.

EPIDEMIOLOGY

The disease is most prevalent in the tropics and subtropics but *Entamœba histolytica* has a world-wide distribution. For instance, a survey in Britain by Dobell in 1921 showed that probably between 7 and 10 per cent. of the population were healthy carriers. Indigenous amœbic dysentery is uncommon in the British Isles, but must always be borne in mind in cases of ulcerative colitis. Different strains of *E. histolytica* may vary in virulence, and it has been suggested that symptomless carriers are infected with non-pathogenic strains, but this suggestion has been disproved as the result of animal experiments. Again, there is no agreement regarding the relative virulence of strains having small cysts, believed by some to be less virulent, and those with large cysts. In fact, no-one has disproved the original work of Walker (1911) and Walker and Sellards (1913) in the Philippines, who showed that in determining its pathogenicity the susceptibility of man is a more important factor than the variation in virulence of *E. histolytica*. The environment which the amœbæ find in the intestine, particularly the bacterial content, may be a factor. Vegetative amœbæ, which are passed when the intestinal symptoms are acute, are short-lived outside the body, and it is generally believed that if they are swallowed by man they are destroyed by the gastric secretions, although animals have been infected successfully in this way. The cysts, however, which are passed when the acute dysenteric symptoms abate, are hardy and live for several weeks if kept moist and cool. The healthy or convalescent carrier is therefore the usual source of infection, apart from certain lower mammals, such as monkeys and rats, which may transmit the disease.

Carriers often pass large numbers of cysts, which may give rise to outbreaks of amœbic dysentery if they find their way into water supplies or

moist food. Bad sanitation resulting in massive infection is more important than climate in the localization of the disease in the tropics and subtropics. The now famous Chicago epidemics of 1933 and 1934 were found on investigation to be the result of water pollution. In the tropics the disease becomes more prevalent during the rainy season, soil polluted with cysts being washed into wells and springs, and after the rains flies increase. Again, in the East, human excreta are widely used for the fertilization of vegetable gardens, so that enticing articles of food, such as strawberries, salads and lettuce, may be heavily contaminated. Most of the worst cases of chronic amoebic dysentery encountered·in this country during the recent war had been invalided from India and dated from the disastrous fall of Burma in 1942, when many men escaping on foot developed dysentery during their long trek. Appalling hardships were suffered along the refugee route, where many died of starvation, malaria, dysentery and cholera, and there was little possibility of sanitation or purification of water.

PATHOLOGY

Most persons infected with *E. histolytica* are healthy carriers and live with their parasites in a state of equilibrium. When this equilibrium ceases or does not exist ulceration occurs in the bowel, normally in the large intestine, the amoebæ multiplying and passing deeply into the tissues, breaking through the muscularis mucosæ. In the submucous layer they undermine the mucous membrane and produce characteristic button-hole ulcers. These may coalesce and lead to large ulcerated areas, when secondary bacterial infection from the intestine takes place. In severe cases the muscular coat may be perforated, resulting in general peritonitis or local adhesions and abscesses. There may be tumour formation, usually in the rectum, cæcum, or colonic flexures. This is the result of amoebic invasion of the bowel, together with a superadded pyogenic infection causing a progressive inflammatory lesion (Morgan, 1944). The inflammation spreads through the bowel into the surrounding tissues, and the resulting mass consists of fibrous tissue, granulation tissue and varying degrees of ulceration. Small abscesses may be present inside the mass. Although such tumours may disappear in a dramatic way after treatment, obstruction may ensue from secondary infection and fibrosis. Strictures may also result from perirectal abscesses. During the past two years I have found an incidence of 1 per cent. of rectal strictures in a series of 700 invalids from overseas with chronic amoebic dysentery in various stages.

The liver is always liable to attack by invading amoebæ which may enter the blood stream and pass from the bowel wall through the portal vein to the liver, where they may colonize, causing hepatitis or abscess. Abscesses may be single or multiple and may occur in any part of the liver, but most commonly a single abscess occurs in the right lobe. Typically, the pus

contained by the abscess is reddish-brown, composed mainly of necrotic liver cells, but it may be frankly purulent although usually sterile. Amœbæ may pass from the liver in the systemic circulation, reaching other organs where they may colonize and form abscesses; for instance in the lungs or the brain.

INTESTINAL AMŒBIASIS

This short consideration of the pathology of the disease cannot fail to emphasize how variable the lesions may be. The symptoms of intestinal amœbiasis are even more variable, and practically any gastro-intestinal disorder from mild dyspepsia to malignant disease may be simulated. The disease process may be so acute that large portions of mucous membrane become gangrenous and slough, but this is exceptional and most cases fall into the chronic category. The term dysentery when used strictly denotes the passage of blood and mucus from the bowel, which is an important but by no means invariable part of the clinical picture. Recurrent bouts of diarrhœa often alternating with constipation are a common feature and sometimes, strangely enough, constipation may be the main complaint. Again, extensive ulceration has been found on sigmoidoscopy in patients with normally formed stools. Payne (1945) has recorded a fatal case of this type. He points out that amœbic typhlitis may be of importance in the differential diagnosis of appendicitis in men who come home from India. In some 50 of his cases there was no dysentery and the presenting symptom was pain in the right iliac fossa. Many cases of amœbiasis have been operated upon mistakenly for appendicitis. There were 13 deaths in 32 such cases in one of the Chicago epidemics (Strong, 1945). The average patient invalided home during the war with chronic amœbic dysentery had recurrent attacks of diarrhœa with blood and mucus accompanied with colicky pain. Between these attacks the stools were semi-formed and contained some mucus. There was often loss of weight and anæmia and sometimes low-grade pyrexia. Usually the cæcum and descending colon, and often the liver edge, were palpable and tender.

DIAGNOSIS.—This rests upon the identification of *E. histolytica* in the stools or in specimens obtained through the sigmoidoscope or the proctoscope. In chronic cases repeated examinations of stools for cysts are often necessary, and at least six specimens should be examined on consecutive days by an expert before a negative diagnosis is pronounced. If there are dysenteric symptoms the stools should be examined for active amœbæ when fresh and warm. The cellular exudate is of little significance and the presence of Charcot-Leyden crystals, although suggestive, is not diagnostic.

Sigmoidoscopy has been shown to be a diagnostic procedure of the greatest importance in amœbic dysentery, for lesions occur in the rectum and sigmoid in over 80 per cent. of cases (Manson-Bahr, 1943), and amœbæ can be found on immediate microscopic examination of scrapings taken from

these lesions. As already mentioned, the degree of ulceration seen through the sigmoidoscope does not always correspond with the severity or duration of the symptoms. The lesions vary considerably in size and appearance. There may be small hyperæmic areas with central yellowish spots scattered in an otherwise normal mucous membrane, or obvious ulcers which may be solitary or multiple, the surrounding mucosa being injected and swollen and giving the ulcers an appearance of depth. Sigmoidoscopy should always be preceded by digital examination of the rectum. If this is not done palpable carcinomas may be missed, as superficially they may resemble amœbic lesions. The sigmoidoscope is also a useful guide in the treatment of patients with ulcers within its reach, as their progress can be watched. The knee-chest position is easiest for the operator, but if the patient is too ill to maintain this the lateral position is usually employed. In many cases proctoscopy may be sufficient; 50 per cent. show lesions in the rectal ampulla (Payne, 1945).

TREATMENT.—Many drugs have been used in the treatment of amœbiasis, often being introduced with phenomenal claims which further experiences have not substantiated. These claims have usually been made on empirical grounds without any testing of the drugs by expert protozoologists. The most generally used drugs to-day are emetine and its compounds, the iodine-oxyquinoline compounds and the organic arsenicals.

No drug has yet been found to compare with *emetine* as an amœbicide. In controlled experiments amœbæ are unable to live after three or four days in concentrations of even less than 1 part of emetine hydrochloride in 5,000,000. Given by subcutaneous injection as instituted by Rogers (1912) it has a dramatic and curative action in amœbic hepatitis and other secondary lesions, for instance in the lungs. In dysentery, however, although emetine injections relieve the acute symptoms they only cure a small proportion of gut infections, and there is still no drug which can be depended upon to do so by itself. It seems unlikely that any one drug will ever cure all cases (Hargreaves, 1946). Since lesions are so variable, no two series of cases can ever be strictly comparable. In the early case the amœbæ in the bowel may be easy of access for drugs, but later these may be prevented from reaching the organisms as the result of inflammatory changes. The best chance of cure at present is by the use of a combination of the most effective drugs available.

Emetine bismuth iodide (EBI), 3 grains (0.2 gm.) given on twelve consecutive nights as a loose powder in gelatin capsules containing 1 grain (65 mgm.), as recommended by Dobell and his co-workers (1918), seems to be the most satisfactory basis of treatment. The patient should be in bed and only a very light diet should be taken a few hours before the drug is given. To minimize the unpleasant effects, a sedative, such as phenobarbitone soluble 1 grain (65 mgm.), should be given half-an-hour before EBI. Daily retention enemas of *chiniofon*, 2½ per cent. in 7 ounces (200

FIG. 1.—Shows almost complete excavation of the right lobe   (By kind permission of Dr Eric Samuel)
RADIOLOGICAL APPEARANCES OF HEPATIC ABSCESS BEFORE AND AFTER ASPIRATION WITH AIR REPLACEMENT.
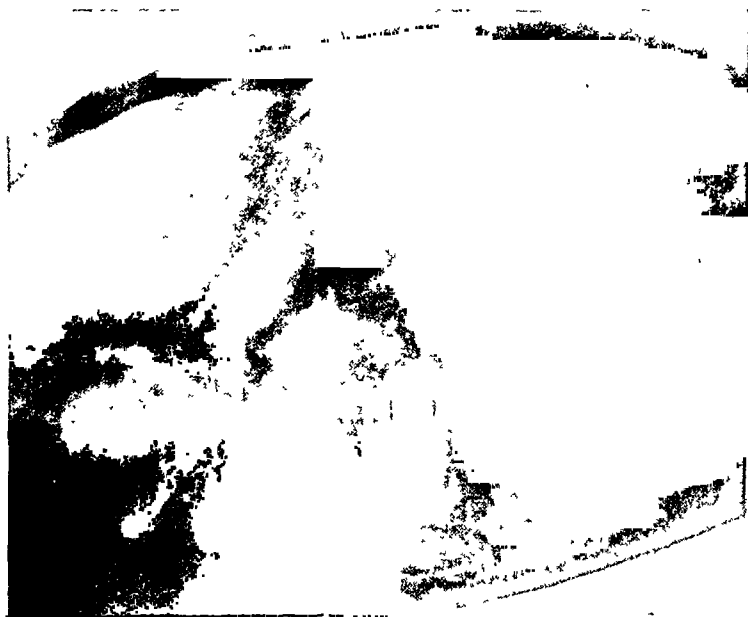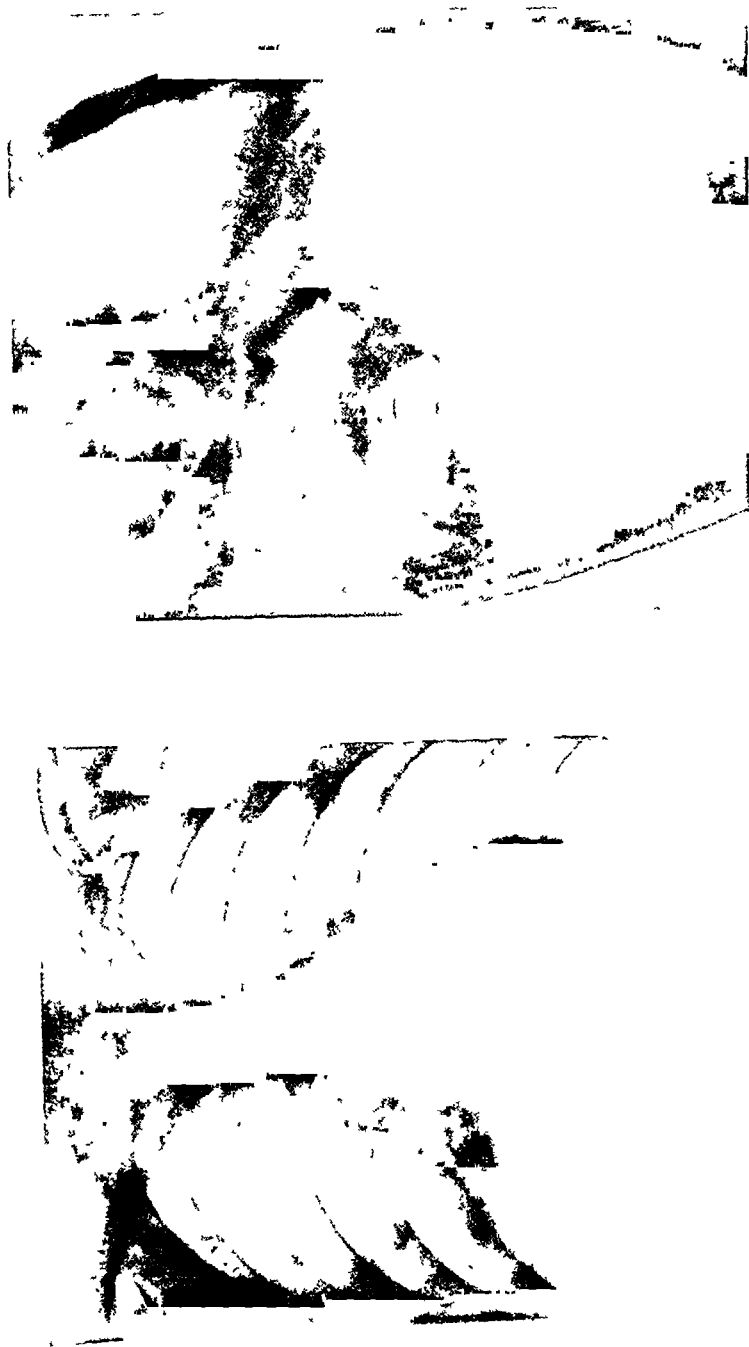
FIG. 2.—Shows a smaller abscess posteriorly in the upper part of the right lobe, seen best in the lateral view. (By kind permission of Captain H. J. Hagger).
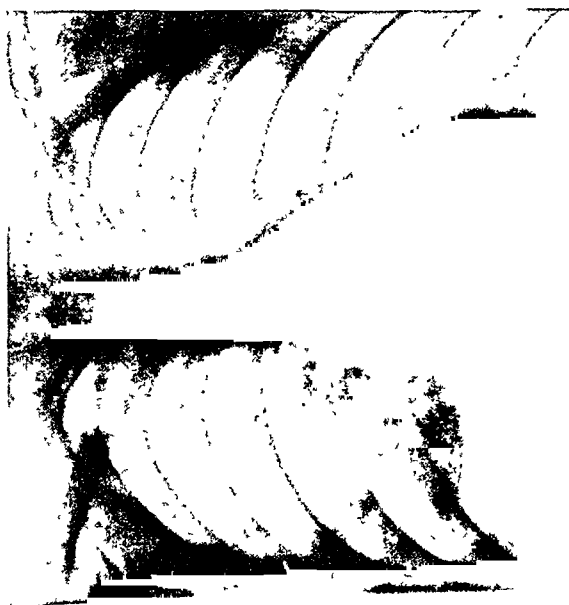
RADIOLOGICAL APPEARANCES OF HEPATIC ABSCESS BEFORE AND AFTER ASPIRATION WITH AIR REPLACEMENT.

c.cm.) of warm water, given throughout the course of EBI have been shown by Manson-Bahr (1944) to be efficacious, and this combined course is widely used. In cases with acute dysenteric symptoms, injections of emetine should be given before the combined course: six daily injections of 1 grain (65 mgm.) are adequate, and at the same time it is rational to give sulpha-guanidine or sulfasuxidine by mouth to combat bacterial infection (Marriott, 1945). After the EBI and chiniofon, a twenty-day course of *diodoquin* should be given, 3 tablets [3.2 grains (208 mgm.) each] thrice daily. This is the newest of the anti-amœbic drugs and was introduced in America in 1935. Although it has not been found as effective as originally claimed, it appears to be the best of the oxyquinoline compounds (Morton, 1945). Diodoquin is now being produced in this country under its chemical name, *di-iodo-hydroxyquinoline*, but if it is not available a course of one of the organic arsenicals, e.g. *carbarsone* or *stovarsol*, 4 grains (0.25 gm.) twice daily for twelve days, should be given in its place.

Tests of cure should be carried out one month after the end of this treatment, six daily specimens of stool being examined and sigmoidoscopy repeated.

Diet.—Fluids only may be tolerated if there are acute dysenteric symptoms, but a high calorie diet should be given as soon as possible. The maintenance of good nutrition and attention to the vitamin intake, especially the B group, is more important than the need for a low residue diet (Payne, 1945).

REFRACTORY CASES OF CHRONIC AMŒBIC DYSENTERY

During the recent war many severe cases were invalided home in which repeated courses of treatment had been given without success. Secondary bacterial infection was found to be an important factor in refractory cases and the use of penicillin proved life-saving in some instances. Such cases are rendered more amenable to anti-amœbic treatment if this is preceded by a course of penicillin parenterally and sulfasuxidine by mouth (Hargreaves, 1945).

Amœboma.—As already described, in chronic cases inflammatory masses may develop in the rectum or colonic flexures. These may present as abdominal tumours or they may be felt or seen in the rectum. When a local mass develops it may be mistaken for malignant disease (Ogilvie, 1945). In the colon the differential diagnosis is not possible radiologically, and in the rectum, where the tumour can be felt and seen, even when amœbæ are found in the stools, a biopsy is indicated to exclude carcinoma, for the two diseases may coexist. Emetine is most valuable in diagnosis, for in the early stages of amœboma formation the whole mass may melt away during a course of injections. Later this may be prevented by a secondary infection; in this event, emetine may prove effective after a course of penicillin.

Fig 2 —Shows a smaller abscess posteriorly in the upper part of the right lobe, seen best in the lateral view.
(By kind permission of Captain H J Hagget)

RADIOLOGICAL APPEARANCES OF HEPATIC ABSCESS BEFORE AND AFTER ASPIRATION WITH AIR REPLACEMENT.

subphrenic abscess may be particularly difficult. Serous and purulent pleural effusions are not uncommon.

Radiographic examination of the chest is often diagnostic. In the early stages diminished movement of the right side of the diaphragm on screening may be the only definite sign. Localized doming seen in the postero-anterior or lateral view indicates abscess formation but often, even in the case of relatively small abscesses, the whole of the right side of the diaphragm is raised and the cardio-phrenic angle obliterated. The outline of the right diaphragm may be blurred as compared with the opposite side. During aspiration, air often leaks in and replaces the withdrawn fluid, the abscess then being easily seen with a fluid level. To make certain of this, air can be introduced purposely so that the abscess can be outlined accurately (see fig. 1 and 2 on plates facing p. 96-7) and its subsequent progress watched in serial films (Cameron and Lawler, 1943).

The liver is usually palpable and tender. An abscess of the anterior and lower part of the right lobe produces a swelling on the right side of the epigastrium. In the left lobe of the liver an abscess may give rise to a tender tumour in the epigastrium. Such abscesses may rupture into the peritoneum, often with fatal results, or into the stomach or bowel, when spontaneous recovery may follow. Sometimes they may cause acute abdominal symptoms, only being diagnosed on laparotomy.

TREATMENT.—Most cases of hepatitis respond rapidly to daily subcutaneous injections of 1 grain (65 mgm.) of emetine hydrochloride given on twelve consecutive days, the tenderness diminishing and the pyrexia subsiding in a few days. In the absence of a definite tumour or radiological signs there is no means of distinguishing clinically between hepatitis and an abscess, and small abscesses may be absorbed following emetine treatment. In cases with definite abscesses, emetine may give symptomatic relief, and it is customary to start the course of injections a few days before aspiration, which is the best method of evacuation. Secondary infection used to call for an open operation, but modern antibacterial agents have diminished this necessity.

Aspiration.—For the usual abscess in the upper part of the right lobe, the liver is explored under local anæsthesia through one of the lower inter-costal spaces in the posterior or mid-axillary line or at the point of maximum tenderness. A long needle is necessary and its bore should be wide as the pus is usually creamy in consistency. The average amount of pus aspirated is about half a pint, although several pints may sometimes be obtained. At the end of the aspiration, 1 grain (65 mgm.) of emetine hydrochloride should be injected into the cavity. The course of twelve emetine injections should be completed and both aspiration and emetine must be repeated if pus re-accumulates. In view of the tendency of these cases to relapse, Hurst (1944) considered it justifiable to give further courses of emetine injections three, six, and twelve months later.

If these measures fail, surgery must not be delayed. Morgan (1944) removed a cæcal mass from a patient with chronic amœbiasis, and even when it was removed it was thought to be an amœboma, but microscopic examination revealed that it was an adenocarcinoma.

AMŒBIASIS OF THE LIVER

Provided the diagnosis is borne in mind, cases of amœbic liver abscess and the prodromal stage of hepatitis should not as a rule be missed. There is little difficulty when the condition develops during or shortly after dysenteric symptoms, but it may not occur until years after the patient has left the tropics, and there may be no history of previous dysentery. Again, the classical clinical picture is easily recognized, but frequently the disease may simulate other conditions or may present obscure general symptoms, such as vague fever with no localizing features.

DIAGNOSIS.—The onset may be insidious or acute, and even fulminating when the whole liver is riddled with collections of pus. The last condition is rarely seen outside endemic areas, and in this country the symptoms may vary from chronic ill health with loss of weight to a sudden episode suggestive of right basal pneumonia or an acute abdomen in a previously healthy patient.

A remittent fever rising to 103° or 104° F. (39.4° or 40° C.) at night is a typical feature in severe cases, but in more chronic ones it is less marked and may subside even when an abscess is present. A low-grade fever with night sweats may be the only symptom. As might be expected, a high leucocytosis with considerable increase in polymorphonuclear cells is often found in cases with marked fever, but again no hard and fast rule can be stipulated, and a normal white cell count does not eliminate the presence of an abscess. The skin often becomes muddy coloured, but frank jaundice is rare. Discomfort and a sense of heaviness in the right hypochondrium are common symptoms, but in severe cases the pain may be so great that the patient cannot lie on his left side, owing to the dragging sensation due to change of position. Pain is often referred from the right side of the diaphragm to the right shoulder, and accentuated by any jarring movement. In abscesses of the left lobe of the liver the pain may be referred to the left shoulder.

Since the upper part of the right lobe is most frequently involved, physical signs at the base of the right lung are of particular significance in patients who have lived in the tropics. Suggestive signs are diminution of movement and vocal fremitus, upward extension of the liver dullness, feeble breath sounds and pleural friction. Later, the lower intercostal spaces may bulge and tender spots may be elicited. An abscess may rupture into the lung suddenly, when the contents are often coughed up, or a chronic basal condition may occur with clubbing of the fingers, giving rise to mistaken diagnoses, such as carcinoma or tuberculosis. The differentiation from

SURGERY IN THE TROPICS

BY BRIGADIER D. FETTES, O.B.E., M.B., F.R.C.S.E.

Honorary Surgeon to H.M. The King; Consulting Surgeon to the British Army.

TROPICAL surgery was a closed book to many surgeons six years ago; but to those who have served in tropical lands the study of this branch of surgery has proved fascinating, and many now at home are consequently much more able to recognize and treat the late sequelæ of tropical diseases in the demobilized armies.

The Service is the best possible training ground. The medical officer, in peace and war, during his career, may serve for many years in all parts of India, for a few years in Egypt, in odd corners of Africa, for a spell of years in China, and in every near and middle east country from the Balkans to Afghanistan. He learns in a hard school, all the faster if perforce in his early days he finds he must do many of his own laboratory investigations himself, all the better if, as sometimes happens, he can study the signs and symptoms in his own body and provide his own pathological specimens. The discomfort of a Sam Browne belt on his right side may teach him volumes.

The tropical surgeon must at once realize that although modern air-conditioning of theatres and wards is some protection against post-operative catastrophes, there is a time and a place for surgery, and the time for cold surgery is not during the hot weather in a tropical land—a death from heatstroke following an operation for hernia is a salutary lesson. He must also realize that just as any operation on a shocked gunshot wounded man is foredoomed to failure unless there is adequate pre-operative resuscitation, so also in emergency tropical surgery the dehydrated sick man must also have his loss made good before he is subjected to even a minor operative procedure. He must modify the ideas he brings from home to suit both conditions and patients: the proved methods at home may not be the methods of choice abroad. However much, for example, the surgeon may disapprove of the use of coagulants in the treatment of burns, he may be forced to the conclusion that in the case of severity under real heatstroke conditions the only thing that matters is that he employ a method which will allow every square inch of undamaged skin to function; he may therefore have to choose between the risk of subsequent infection or immediate death. However obsolete he may consider certain types of amputation, he will find that many natives prefer to hobble on a Syme or other foot stump than walk delicately on the best artificial limb, and the climate will deal much more kindly with his stump than will the cold and damp of a more northerly clime. He may on occasions be shocked to find that some of his native patients regard a stump as nothing less than a veritable copper mine, and the more revolting its aspect the better. The native's reactions are in fact often unpredictable: moribund, he can recover from operations of the utmost magnitude, or succumb for no obvious reason to an operation which is not in the least serious. He can recover the most complete function in

Occasionally pus is not present, and the hepatic enlargement subsides completely with emetine. Again, only small beads of pus may be withdrawn at varying depths, suggesting multiple small foci, and here again emetine by itself has effected a cure. In fact the action of emetine is so specific in amœbic hepatitis that it is commonly diagnostic of the condition, and its trial is justified in patients with a previous history of dysentery or residence in the tropics who complain of hepatic pain for which no cause can be found on investigation. Sometimes a raised sedimentation rate may be the only indication of an active disease process, falling to normal limits after emetine treatment. If *E. histolytica* is found in the stools the emetine injections should always be followed by a course of treatment for the bowel infection.

References

Cameron, J. D. S., and Lawler, N. A. (1943): *J. roy. Army med. Cps.*, 80, 1.
Dobell, C. (1921): *Med. Res. Coun. Spec. Rep. Ser.*, No. 59.
——, Gettings, H. S., Jepps, M. W., and Stephens, J. B. (1918): *Ibid*, No. 15.
Hargreaves, W. H. (1945): *Lancet*, ii, 68.
——, (1946): *Quart. J. Med.*, 15, 1.
Hurst, A. (1944): "Medical Diseases of War", London.
Manson-Bahr, P. H. (1943): "The Dysenteric Disorders", London.
——, (1944): *Lancet*, ii, 718.
Marriott, H. L. (1945): *Ibid*, i, 679.
Morgan, C. N. (1944): *Brit. med. J.*, ii, 721.
Morton, T. C. St. C. (1945): *Ibid.*, i, 831.
Ogilvie, W. H. (1945): *Lancet*, ii, 585.
Payne, A. M. H. (1945): *Ibid.*, i, 206.
Rogers, L. (1912): *Brit. med. J.*, i, 1424.
Strong, R. P. (1945): "Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases", London.
Walker, E. L. (1911): *Philip. J. Sci.*, B. 6, 259.
——, and Sellards, A. W. (1913): *Ibid.*, 8, 253.

sometimes encountered—I can recall a case of amœbic hepatitis complicated by double pneumonia in which the leucocyte count was 130,000.

Malaria often appears first on the list of diseases which may mimic a surgical condition. It certainly is important that the possibility of this disease alone or as a complication should never be forgotten at any stage of an illness which appears to be, or is, surgical. It may be a relief to know that an alarming sequence of post-operative events is malarial in origin, but it will save much wear and tear to both patient and surgeon if the possibility is foreseen and the attack prevented. The diagnosis of abdominal malarial states should not present very great difficulties if it is remembered that any abdominal organ may suffer the acutest congestion, even necrosis, from occlusion of its blood vessels by parasites. When an acute malarial spleen is seen and handled it appears surprising that rupture does not occur oftener; the pain, tenderness and guarding over a spleen which is not even palpable, can be marked, and there must often be the suspicion that even in the absence of any trauma a malarial spleen is leaking. The case may need careful watching for many days and the diagnosis may be *really* difficult, *the* condition may resemble a firework rocket which fizzles, appears to peter out and then goes off with a roar. It is important also not to accept the enlarged congested liver in a malaria case as being necessarily a malarial manifestation; many an amœbic abscess has been present in addition, and has been missed.

In the early stages there should be no great difficulty from the surgical point of view in the diagnosis of *typhoid*. In all tropical fevers in which the Peyer's patches are grossly involved, the surgeon will be called in because of the right iliac signs. Many cases recognized as typhoid have been operated on because the surgeon has been in such doubt. In the early stages an appendicectomy does not appear to affect the case deleteriously but the history and the leucopenia should be sufficient to contraindicate operation. In none of these tropical conditions should an appendicectomy ever be performed unless there is a certainty that an appendicitis is not only acute but is obstructive. The surgeon who has himself suffered the pain of an obstructive appendicitis is unlikely ever to operate on doubtful cases of this type, the character of this pain bears no resemblance to the severest intestinal colic, no resemblance to the spasms in acute dysentery, it suggests to the sufferer nothing less than that his bowel is being crushed in a grinding mill. In the not so late stages of the illness the diagnosis of perforation may be obvious, but in the terminal stages when meteorism is maximum and toxæmia profound, it may be a very different matter. In patients too moribund for any operation there may appear to be quite convincing signs of perforation, yet subsequent post-mortem examinations reveal none.

So also in *other fevers*, in sandfly and dengue, the surgeon may be asked for an opinion. Many a journey does he make to the case of imminent heatstroke with abdominal pain. There is seldom an epidemic of typhus of any severity without an abdomen or two being explored. The unnecessary exploration may be serious, it will tip the scales in typhus, it will have dire

what appears to be a hopelessly damaged limb, or he may refuse ever again to flex his normal knee joint after quite a perfect removal of a torn cartilage. He requires far more supervision than any patient at home. He can be expected, if given the opportunity, to remove by brute force his operation dressings or a plaster jacket, to extract, also by brute force, any tube, whether it be draining his cerebral abscess or his ileum. If he is missing from bed twelve hours after having had his middle meningeal artery tied, he will be found two hundred yards away, looking for something, and in all probability will come to no harm from his escapade.

These occurrences enliven the daily round of the surgeon in the tropics. By the time he has had to fight heatstroke in his surgical cases not due to tropical disease, and has been called in to operate on every type of tropical fever, he will learn how few indeed are the diseases met in the tropics which have no surgical aspects.

As regards tropical diseases, in the Service the surgeon starts off with a knowledge of general tropical medicine, he learns afresh the diseases endemic in that country to which he is posted; in Egypt therefore he should not be caught napping by a case of bilharziasis, and he may not be caught when a case of the same disease turns up from Africa in India when least expected. In the next country he visits he may learn all he needs to know about filariasis; he may learn that there is no contraindication to his operating on filarial hydroceles, but he will also learn that his native patient may regard as grievous bodily harm any operative procedure which leaves him with a testis the size of a walnut instead of one of which he had been very proud. Tropical diseases such as those mentioned are a matter of book work and experience, and are not necessarily difficult problems, but there are many conditions—mostly abdominal—which can be puzzling both as regards diagnosis and treatment.

ABDOMINAL CONDITIONS: DIAGNOSTIC DIFFICULTIES

In every doubtful abdominal case three points should be considered:— (1) Is the disease, which appears to be surgical, a purely medical complaint? (2) is there a surgical complication of a medical disease present, and (3) are two diseases present?—very often there are. The history is of great importance, a suspected *appendicitis* in which there is an upset of the common sequence of generalized then localized pain and of vomiting following pain should be viewed with suspicion; it requires much investigation before it can be regarded as entirely surgical. Then there is no reason why an appendicitis patient should not have a headache, but in the tropics it should give one furiously to think! The blood picture is often the other most useful aid and a blood examination must be routine in all abdominal cases for it may give evidence that malaria at least is partly responsible for the abdominal state. It can also be expected in the tropics that the white cell count will give good information—6,000 means a medical fever; 12,000 with a dry furred tongue, more than suggests the appendix which is gangrenous; a total around 20,000 should draw attention to the liver; a freak leucocytosis is

any form of medical treatment, and which after weeks or months is emaciated to the point of death. Cæcostomy as a last resort in some of these cases can be spectacular in its results, and there can be few rewards in surgery to equal that of the metamorphosis of a Belsen-like creature into a flourishing young woman. This form of treatment also had its successes amongst the victims incarcerated in Thailand, even when conditions were difficult beyond belief.

A little space must be given to the *amœbic granuloma*. Many years ago it was a most puzzling occurrence when a case of inoperable carcinoma of the rectum, colostomized and sent home to die was reported later to have made a complete recovery. Some such cases may have been lymphogranulomatous, most were amœbic in origin. In a land where amœbiasis is rife these cases are prevalent and it is wise not to claim any great ability to recognize their true nature, for the case which appears beyond all shadow of doubt to be carcinoma may respond happily to emetine treatment, and unhappily *vice versa*. The patient with a granulomatous mass in the rectum or a little higher up, or in the cæcum, smooth or craggy, ulcerated or not ulcerated, should be put on an emetine test, and have a biopsy done. In the early stages emetine will cure the condition, later emetine and chemotherapy may be successful in overcoming both the underlying and the secondary infection but, as Naunton Morgan has pointed out, surgery may be required to overcome the permanent mechanical distortion which may result, and may also be the only way of determining that a carcinoma is not also present.

Another precept which all tropical surgeons have learned in this war is that there must be no operation, however small, on the anal canal within two months of an attack of diarrhœa; before any such operation, the possibility of amœbic infection must be excluded by sigmoidoscopy and stool examinations. Emetine should be given a trial in any perianal ulceration.

Hepatic abscess.—It has already been advised that in the tropics, three points should be considered in the investigation of any abdominal condition of any obscurity; a fourth might well be added: let the surgeon always ask himself the question "is there any possibility of this being an abscess of the liver?" It is seldom that any tropical hospital is visited without at least one case coming to light which might very easily be an hepatic abscess but in which that possibility has been overlooked. The symptoms may be classical and the diagnosis easy. On the other hand, a man may die, having shown no muddy look, no obvious liver enlargement, no leucocytosis, no radiological signs, no fever or only a pyrexia of the typhoid or malarial type. There may be only right basal signs, loss of weight, and night sweats; an extension of the abscess into the thoracic cavity may further concentrate the attention on the lung; the rigors and liver enlargement may cloud the issue still more and be held as verification of a diagnosis of malaria; early jaundice, from pressure or toxæmia may be regarded more as evidence of other hepatic conditions; subphrenic or perinephric abscess may appear to be a likelier explanation; the left lobe abscess may, as the result of pressure, give radiological signs which in an emaciated man of cachectic appearance appear to be complete verification of a diagnosis of gastric carcinoma. If

results in the obscure pyrexial case suffering from various deficiencies; such a patient, explored because of vague obstructive signs, dies later with his laparotomy wound showing no trace of healing.

These diseases all present difficulties to the medical officer, and sometimes to the surgeon, but probably more puzzling are those abdominal states which are connected with the dysenteric infections.

SURGICAL INTERVENTION IN AMŒBIASIS

The amœbic ulcer which perforates is not so very rare, its signs and symptoms may be unmistakable as in acute perforation of a viscus elsewhere, its treatment may be a difficult matter by reason of the state of the bowel. Equally often the perforation will be much more insidious and a retroperitoneal or circumscribed abscess will form and will sometimes evacuate itself into the bowel.

The differential diagnosis of *amœbic typhlitis and appendicitis* is sometimes far from easy. An unnecessary exploratory operation may be fraught with the danger of setting up hæmorrhage which may be very serious, and the danger also is described of amœbic infection of any sinus which may develop, or of the skin, but this latter complication is unlikely except in a case unrecognized and untreated as amœbic.

It occasionally happens that during the acute stage of a severe amœbic dysentery, masked by the other symptoms present, a fulminating appendicitis occurs. When many cases of dysentery are being admitted the right iliac mass is by no means an unusual feature. As a rule it responds to expectant treatment as quickly as would an ordinary appendicular abscess, and on many occasions, later operation has revealed the typical leather-like inspissated remnants of an abscess around a burst appendix. Why such a case should tend to localize is not clear, for the bowel cannot be put at rest adequately during the acute stage of a dysentery. It appears reasonable to infer that if an appendix is unhealthy, and contains a large concretion, any local congestion, such as acute dysentery can cause, may lead to serious interference with its circulation, thus precipitating an attack of obstructive appendicitis. In dysentery and other tropical diseases, every effort within reason should be made to avoid operation, but even if a proved amœbic infection be present, operation should not be withheld, if the history is correct for appendicitis, the pain is of the characteristic type already described, a leucocytosis is present, and the case is early, i.e., within forty hours. Any operation must be carried out with excessive gentleness, and if by any chance the appendix is found to be inflamed, only as part of a more extensive process, but is not obstructed, it will be wise to refrain from removing it. After forty hours the right iliac mass should be treated on the Ochsner-Sherren lines, "on the threshold of the theatre", and an emetine course given if amœbiasis is proved or suspected. If operation becomes imperative the minimum should be done.

More seldom in the future than in the past, there will be the occasional case of dysentery other than amœbic which tragically does not respond to

any form of medical treatment, and which after weeks or months is emaciated to the point of death. Cæcostomy as a last resort in some of these cases can be spectacular in its results, and there can be few rewards in surgery to equal that of the metamorphosis of a Belsen-like creature into a flourishing young woman. This form of treatment also had its successes amongst the victims incarcerated in Thailand, even when conditions were difficult beyond belief.

A little space must be given to the *amœbic granuloma*. Many years ago it was a most puzzling occurrence when a case of inoperable carcinoma of the rectum, colostomized and sent home to die was reported later to have made a complete recovery. Some such cases may have been lymphogranulomatous, most were amœbic in origin. In a land where amœbiasis is rife these cases are prevalent and it is wise not to claim any great ability to recognize their true nature, for the case which appears beyond all shadow of doubt to be carcinoma may respond happily to emetine treatment, and unhappily *vice versa*. The patient with a granulomatous mass in the rectum or a little higher up, or in the cæcum, smooth or craggy, ulcerated or not ulcerated, should be put on an emetine test, and have a biopsy done. In the early stages emetine will cure the condition, later emetine and chemotherapy may be successful in overcoming both the underlying and the secondary infection but, as Naunton Morgan has pointed out, surgery may be required to overcome the permanent mechanical distortion which may result, and may also be the only way of determining that a carcinoma is not also present.

Another precept which all tropical surgeons have learned in this war is that there must be no operation, however small, on the anal canal within two months of an attack of diarrhœa; before any such operation, the possibility of amœbic infection must be excluded by sigmoidoscopy and stool examinations. Emetine should be given a trial in any perianal ulceration.

Hepatic abscess.—It has already been advised that in the tropics, three points should be considered in the investigation of any abdominal condition of any obscurity; a fourth might well be added: let the surgeon always ask himself the question "is there any possibility of this being an abscess of the liver?" It is seldom that any tropical hospital is visited without at least one case coming to light which might very easily be an hepatic abscess but in which that possibility has been overlooked. The symptoms may be classical and the diagnosis easy. On the other hand, a man may die, having shown no muddy look, no obvious liver enlargement, no leucocytosis, no radiological signs, no fever or only a pyrexia of the typhoid or malarial type. There may be only right basal signs, loss of weight, and night sweats; an extension of the abscess into the thoracic cavity may further concentrate the attention on the lung; the rigors and liver enlargement may cloud the issue still more and be held as verification of a diagnosis of malaria; early jaundice, from pressure or toxæmia may be regarded more as evidence of other hepatic conditions; subphrenic or perinephric abscess may appear to be a likelier explanation; the left lobe abscess may, as the result of pressure, give radiological signs which in an emaciated man of cachectic appearance appear to be complete verification of a diagnosis of gastric carcinoma. If,

therefore in any obscure chest or abdominal condition there are right basal signs, if a malaria case is not responding to treatment, if any patient is going downhill from no discoverable cause, these are all urgent indications for thorough investigation: blood counts, sigmoidoscopy, stool examinations, radiological examinations, therapeutic emetine test, adequate and repeated explorations of the liver. When exploring, a fairly wide-bore needle should be used, and if pus is struck it is advisable to aspirate as much as possible there and then, until some idea of the size of the cavity is obtained: a large abscess requires an aspirator but if the abscess is a small one a second attempt to locate it may not be so successful.

If exploration is repeatedly negative in a strongly suspected case an exploratory laparotomy should not be long delayed. Oftener than on the right side, an abscess of the left lobe seems to succeed in evading the exploring needle, but an abscess in that situation amenable to treatment by aspiration will be obvious immediately the abdomen is opened. Twice recently were cases seen—strongly suspected of liver abscess, repeatedly negative to exploration, revealed at once by laparotomy to be left lobe suppurative echinococcal cysts.

The open operation has fallen into some disrepute but in pre-aspiration days it was possible to obtain good results by that method, even though secondary infection was a certainty under the conditions then prevailing and with none of the modern methods of cross-infection prophylaxis now available. Therefore if the aspirated case fails to make the progress expected on emetine and chemotherapy, the question of open operation will require serious consideration, for it is only too easy to wait and hope too long and to proceed to more heroic measures too late.

The same line of treatment holds good in cases of *pulmonary amœbiasis*. Many a liver abscess is coughed up, sometimes with partial success, but it seems a most unsurgical procedure to hope for a secondarily infected hepatic abscess, communicating with the chest through an opening which is probably valvular, to be evacuated satisfactorily through a long tortuous uphill and exceedingly unnatural channel by the patient's own efforts. The disease should be attacked at the source and before it is too late.

CONCLUSION

Tropical surgery is a vast subject and in this short article, an attempt has only been made briefly to describe a few of the difficulties which are everyday occurrences. Surgery in the tropics is largely a matter of postponing the necessary but not life-saving operation for a more auspicious occasion and of excluding from surgery those conditions which are better left to the physician. In the unavoidable operation it is a matter of countering the fluid loss which has occurred before the patient is seen, which may occur seriously during the operation and for some days following it. It is a matter of brooking no delay in those cases in which the indication for urgent surgical intervention is present, however masked that indication may be by tropical conditions or other tropical diseases.

HEATSTROKE AND SUNSTROKE

By J. BALFOUR KIRK, C.M.G., M.B., Ch.B., F.R.C.P.

Late Colonial Medical Service.

The 1914-1918 war gave a great impetus to the study of the effects of heat and sunlight upon the human organism, and more particularly upon those members of the white races not indigenous to the tropics. The war of 1939-1945 has provided a further stimulus for the same type of studies, and some interesting work has appeared which, although it has not materially altered the concepts which were held as a result of the experience gained during the 1914-1918 war and subsequently, has provided data which in certain cases have tended to give greater precision to the appreciation of the factors involved. Nevertheless, there is still much in the phenomena arising from the exposure of the human body to high temperatures and solar radiation which is not yet capable of rational explanation in accordance with ascertained fact.

It will perhaps serve the purpose of this article best if the types of syndrome which have been differentiated on clinical grounds are first described, followed by a short account of what has been thought to be the underlying causes of the clinical findings; and then to review practice in prophylaxis and treatment, based upon modern knowledge.

CLINICAL TYPES

There are five clinical types of reaction of the human body to excessive heat and solar radiation. These may be termed, in order of severity of the first four, (1) simple heat collapse; (2) heat cramps (stokers' cramps, miners' cramps); (3) heat exhaustion; (4) heat hyperpyrexia, and (5) sunstroke. Although this distinction between the different types is fairly clear, it is equally clear that there is a strong family resemblance among them to which reference will be made later.

Simple heat collapse has recently been described by Caplan (1943) as he encountered it among workers in the Kolar gold mines in India. Work in these mines is carried out at great depths; levels 8,700 feet below the surface are mentioned. At such depths temperatures are high. Many miners work in temperatures of 100° F. to 120° F. (37.8° C. to 48.8° C.) dry bulb, and 90° F. to 97° F. (32.2° C. to 36.1°C.) wet bulb. Caplan's account deals with 244 cases which were considered to be due wholly or partly to conditions underground. Of these, 194 were classed as "mild", 41 as "moderate", and 9 as "severe" collapse. The mild cases had almost completely recovered by the time they were admitted to hospital. They gave histories of fatigue, asthenia, giddiness and, less frequently, vomiting, cramp and loss of consciousness. The loss of consciousness was often momentary and was probably never more than of ten minutes duration. Among those patients, 37 per cent. showed hypotension, 26 per cent. reduced pulse pressure, 21 per cent. bradycardia; 67 per cent. of blood examinations showed a plasma.

chloride concentration under 560 mgm. per cent., and 9 per cent. showed a mild dehydration, as indicated by some loss of skin elasticity.

In the classification of his "moderate" and "severe" cases Caplan regarded complete unconsciousness and inability to palpate the pulse at the wrist as the criteria for including the case in the "severe" category. The general clinical picture was one of surgical shock. In both groups the prodromal symptoms already mentioned were always followed by vomiting, cramp and unconsciousness. Visual and aural disturbances were recorded in about half the cases. Vomiting often recurred five or six times, and was followed within a few minutes by cramps of variable severity, usually affecting the extremities but sometimes occurring in the abdomen and trunk. The skin was cold and clammy and the temperature subnormal, the pulse weak or indetectable, and the heart rate 80 to 140 per minute. In severe cases the blood pressure could not be measured; in the moderate cases it was commonly 60 to 90 mm. Hg and always below 95 mm. Hg. Pulse pressures were 2 to 10 mm. Hg. Hæmoglobin estimations were as high as 140 per cent., and red blood counts up to $7\frac{1}{2}$ millions were found. In 86 per cent. of 43 examinations plasma chloride was below 560 mgm. per cent. Blood urea and blood sugar concentrations were within the normal range. There was no death in this series and the patients made a quick recovery.

Heat cramps (syn. Stokers' cramps, miners' cramps).—This condition has been well known for many years and it may be expected to occur when men undertake hard physical work in a high atmospheric temperature, as in the open desert in midsummer, in the stokehold of a ship in tropical seas, in a deep mine or in steelworks.

There may be a prodromal period during which the patient complains of headache, which may or may not be severe, vertigo or uncontrollable twitchings of the voluntary muscles. But the main feature of this syndrome is the occurrence of extremely painful muscular cramps. These may come on while the man is at work, or they may be delayed for a considerable time after he has ceased working. The pain is agonizing; it is accompanied by sweating, pallor and anxiety. The sweating may precede the onset of the cramp and the muscular spasm may last up to two or three minutes. The muscles most frequently affected are those most used in the type of work the patient has been doing. Most commonly, cramps occur in the muscles of the arms, legs or back, but sometimes the abdominal muscles may also be involved. The muscle can be felt as a hard lump when it is in spasm, softening as the spasm wears off. When this happens the pain ceases.

There is no great rise in the temperature of the body and, apart from the anxiety caused by the agonizing pain, the nervous system does not appear to be greatly affected. Vomiting is seldom a prominent feature.

Heat exhaustion.—This syndrome has been recently described by a number of writers, Wolkin, Goodman and Kelley (1944); Allen and O'Brien (1944); Ladell, Waterlow and Hudson (1944). Wolkin's studies were made in

the American desert, Allen's in Northern Australia and New Guinea, and Ladell's in the desert of Southern Iraq and, although the observations were made in such widely distant places, there is considerable measure of agreement among them.

Ladell and his associates distinguish two well-defined types of heat exhaustion, one, seen in the early part of a hot season, which they term type I, the other in the latter part, which they term type II. The *type I* cases conformed generally with the syndrome of simple heat collapse already described. In the great majority of these cases the symptoms did not begin to appear until the daily maximum temperature had exceeded 115° F. (46.1° C.) for three or four days running, and the history was short. The quantity of urine passed in the twenty-four hours was greatly diminished, the volume being often less than 750 c.cm. It was heavily pigmented and the specific gravity frequently exceeded 1020. The biochemical examinations of blood and urine revealed gross salt deficiency.

Heat exhaustion type II.—The incidence of this type seems to be related to the duration of the hot weather and not to the external temperature. The most prominent symptom was defective sweating which was complained of by 87 per cent. of the patients. The patients themselves had noticed that sweating had stopped and that they then became exhausted and dizzy. The stoppage of sweating was confined to certain areas of the body and limbs, the head and neck generally sweating profusely. When the stoppage of sweating had been patchy and of considerable duration the patient had felt increasingly weak and had suffered from dizziness, insomnia and loss of appetite. A common symptom in this group was dyspnœa, which was worse in the middle of the day. In contrast to simple heat collapse, vomiting and cramps were rare and were not severe. Frequency of micturition was extremely common and copious amounts of urine were passed. Nearly half the patients passed urine more than eight times in twenty-four hours.

On admission to hospital the patients did not look ill. They were a good colour, sometimes flushed. Signs of dehydration were considered to be present in only one case. The average pulse rate in the recumbent position was 76 per minute; the pulse volume was always good; the pulse pressure was variable but high values were much more common than low ones. The reaction to standing was normal. The average rectal temperature on admission was 100.9° F. (38.25° C.) and the mouth temperature 99.5° F. (37.7° C.).

One interesting feature of the series of cases under discussion was that 80 per cent. of the patients of type II heat exhaustion had severe or moderately severe prickly heat which, by the time the patient had been admitted to hospital, was in the desquamating stage. The severity and distribution of the desquamation both varied. When desquamation was present the skin was dry to the touch.

The total urinary chloride was high, although actual chloride concentrations were low. The average daily loss of chloride in forty-five subjects for

the first two-and-a-half days was 3.47 gm. (as NaCl). The average urea concentration was 1 per cent. Thirty-one cases of this type showed reduced whole-blood chloride and reduced plasma chloride.

The series of cases reported by Wolkin, Goodman and Kelley showed the same general features as the type II just described. They also describe a fine papular skin eruption and a branny desquamation, although they do not term it prickly heat, nor do they record polyuria. Allen and O'Brien's account resembles those of the preceding two inasmuch as it records cessation of sweating on the body and the occurrence of prickly heat prior to the actual attack. These authors do not mention polyuria, but give an account of certain histological changes in the sweat glands and their ducts leading to occlusion of the mouth of the sweat duct and the formation of a small vesicle in the malpighian layer by cystic distension of the occluded duct, accompanied by lymphocytic infiltration and dilatation of the lymphatics around the duct immediately below the vesicle. They consider that part of the symptomatology may be referable to the abnormal "internal circulation" of the sweat occasioned by these anatomical changes.

Heat hyperpyrexia.—This condition is most frequently ushered in by certain prodromal symptoms. The most distinctive of these are a marked disinclination for exertion, irritability of the bladder, pains in the limbs, mental confusion, general nervous irritability, diminution or lack of knee jerks, associated, of course, with exposure to high atmospheric temperature and great diminution or cessation of sweating.

If the patient is not treated for his condition, or sometimes even at the first indication that there is anything amiss, he passes into a phase of transient restlessness, or perhaps delirium, and rapidly sinks into coma with a rising temperature. By the time he is comatose the rectal temperature may register 107° F. to 108° F. (41.7° C. to 42.2° C.) which brings it within the hyperpyrexial classification. Unless at this point active measures are taken to reduce the temperature, death is merely a matter of hours. When the patient has a weak heart death from acute heart failure may occur even before the hyperpyrexial stage is reached.

Sunstroke is a condition seen in certain persons after exposure to intense sunlight. The ill-effects may vary from mild headache and general lassitude, which wear off after a few hours, to intense headache, dry skin, rapid, full pulse, aversion to light and even vomiting and delirium. All cases exhibit a certain degree of fever which may last for several days. Severe cases may show sequelæ in the form of nervous affections, loss of memory, which may be peculiarly patchy in type, and inability to concentrate on work.

DISCUSSION

The conditions discussed in this article have as a common feature the exposure of the body to amounts of radiant energy for which it has not compensated. The energy may be in the form of heat rays or of sunlight. Although, as has been stated, there is a strong family resemblance among

them, each taken as a syndrome is quite a distinct entity. It is evident that there are many phenomena common to all, the distinction between them lying rather in emphasis than in variety. Thus the patient suffering from heat collapse, in addition to presenting a variety of the generic features, exhibits as his main trouble circulatory failure and other signs of surgical shock. The patient who is going to become hyperpyrexial may show several of the more or less "generic" features but on the other hand he may not, and his main reaction is a sudden, complete breakdown of his heat regulating mechanism leading to the fulminating hyperpyrexia which is such an alarming feature of this syndrome.

A certain amount of work has been done in attempting to assign to each of the different phenomena its exciting cause, but it must be concluded that efforts in this direction have not gone far. There is sufficient evidence, however, for the establishment of a prophylactic and therapeutic regime if the cause underlying such conditions is regarded as mainly involving (a) overheating and (b) dehydration.

The main cause of heat hyperpyrexia is *overheating* of the body associated with failure of the sweating mechanism. To a certain extent this is also true of the type II heat exhaustion, but in that and in the other conditions, except sunstroke, there is dehydration as well to complicate the picture. The dehydration is due to the excessive amount of water and salt lost in the sweat. It is an important factor in heat cramps, simple heat collapse and heat exhaustion.

Dehydration may involve a loss of water without undue salt depletion, although persons who have lived through a hot spell invariably suffer some degree of salt depletion and consequent dehydration because they seldom make up in the diet the equivalent quantity of salt they lost in the sweat. (Marsh 1933; Ladell *et al.* 1944.) The quantity lost, however, does not enter to any great extent into the pathology of water lack in these climates.

The more serious conditions have as their principal basis excessive loss of body chlorides, involving, it is thought, alterations in the electrolytic balance of the tissue fluids of which the clinical phenomena are the outward manifestations, and the variety of these is probably dependent upon individual variations in the capacities of the tissues involved for meeting this severe threat, although the rôle of the individual tissues or organs involved has not yet been elucidated.

<center>TREATMENT</center>

Heat hyperpyrexia.—This must be regarded as an emergency, and treatment applied at the earliest possible moment, as speed may be an important factor in saving life. The immediate object is to bring the patient's temperature to within the normal range as soon as possible. The patient should be brought into the shade, or out of his hot environment, stripped and drenched with water. Promotion of evaporation of the water is then effected by fanning the surface of his wet body, either by power-fans, a punkah, or

hand-fans. In the meantime a sheet is soaked in water, as cool as it can be made, and the patient is enveloped in that, the fanning being continued. These measures will usually suffice to lower the temperature sufficiently to enable the patient to recover consciousness and should be discontinued and the patient wrapped in a dry blanket or bath towel as soon as the rectal temperature reaches 102° F. (38.9° C.), since the fall in temperature continues for some time after discontinuance of artificial cooling. When this has been accomplished the patient will be conscious and he should then be required to drink up to two pints of 0.25 per cent. saline containing 0.1 per cent. potassium bicarbonate. Sweating will probably occur at this stage, and is a favourable sign. It is important that as the temperature falls the pulse should be carefully watched and any tendency to circulatory collapse anticipated by the administration of 2 to 3 c.cm. of a sterile 25 per cent. solution of nikethamide intravenously, or camphor or caffeine subcutaneously. Cyanosis, with engorgement of the veins of the neck, may be relieved by blood-letting, and artificial respiration may be necessary.

As soon as possible the patient should be removed to a cooler environment for further treatment and investigation of any possible complicating factors, such as malarial fever (the most likely exacerbating or exciting cause of this condition in areas where heat hyperpyrexia is endemic). To prevent relapse the patient should be carefully watched during convalescence, during which time he is kept in bed and treated by the administration of saline drinks and powdered NaCl, so that his consumption of NaCl averages not less than 15 gm. daily. The advisability of exposing him again to the conditions under which he contracted his illness should be carefully weighed against the possibility of his transfer to a cooler climate.

Simple heat collapse, cramps, and *heat exhaustion* have as their common basis salt depletion and dehydration. All are benefited by removal to a cool place and by the administration of normal saline, either intravenously or by the mouth. Under such treatment recovery is rapid and generally complete.

Sunstroke.—Patients suffering from sunstroke should be kept in a cool, darkened, well-ventilated room. Wet compresses applied to the head are soothing. The diet should be fluid for the first day or two and alcohol should be forbidden. Restlessness and insomnia may react well to bromides. As soon as convalescence is established the patient should be instructed in the methods of preventing a recurrence by keeping out of the direct sunlight or by protecting his head and neck by suitable headgear if he must venture out in the middle of the day. If the attack has been severe a change of climate to a less sunny country should be advised.

PROPHYLAXIS

In syndromes such as those under consideration prophylaxis is as important as efficient treatment. Among the prophylactic measures which may be instituted, careful selection of the personnel who will be working in high temperatures is a valuable factor. They should be young, physically fit, and

specially tested by sojourn for varying periods in rest rooms under controlled high temperatures. Those who do not respond favourably to such tests, i.e., whose temperature remains elevated for an undue length of time after leaving the room, should not be recruited if this is avoidable. Elderly persons should not venture into the torrid zone in the height of the hot season if they can possibly avoid it.

Nevertheless, even those who pass the initial tests and medical examination require acclimatization to some extent. This is generally effected gradually by taking in recruits during the cool weather or by subjecting them to working conditions in the dangerous environment for short periods at a time, gradually increasing the working time until the worker can perform his full spell without detriment to his health.

Ventilation.—The working places should be well ventilated and kept as cool as possible. This frequently involves engineering and architectural problems which are outside the scope of this brief review. In countries where Europeans are liable to contract heat hyperpyrexia there should be specially cooled treatment wards established in the general hospitals and emergency cool stations for primary treatment in places where the nature of the work tends to cause its occurrence.

Air conditioning, combined with the cooling of houses and offices, is now a common feature in the bigger tropical cities; if a whole dwelling cannot be so treated, at least a living room and bedroom may be done. Where there is no air conditioning a great deal can be done to mitigate the effects of the midday and afternoon sun by careful attention to closing up the house during the early morning, and throwing it open after sundown. The object in this is to prevent hot air from entering during the day and to allow the cool night air to flush the dwelling thoroughly at night. Sprinkling the compound with water frequently in the afternoon is also a useful practice for keeping a house cool in hot dry climates, but is not so successful in humid regions.

The *personal hygiene* of the hot weather requires special attention. Clothing should be reduced to the minimum but head protection is necessary in desert countries when people are outside during the day. About the best headgear is the pith helmet lined with aluminium foil. It is light and cool.

The *diet* should be light and appetizing, and salads prepared from vegetables grown under strict hygienic supervision should form a substantial part of it, as should also fruit to counteract any tendency to constipation. Plenty of bland fluid must be taken, but alcohol in moderation and then only in the evening. Light beer may be consumed with lunch. Tea forms an acceptable drink and iced coffee may compete favourably with "mineral waters".

References

Allen, S. D., and O'Brien, J. P. (1944): *Med. J. Aust.*, **31**, 335.
Caplan, A. (1943): *Bull. Inst. Min. Metal.*, **463**, 1.
Ladell, W. S. S., Waterlow, J. C., and Hudson, M. F. (1944): *Lancet*, ii, 491.
Marsh, F. (1933): *Trans. roy. Soc. trop. Med. Hyg.*, **27**, 255.
Wolkin, J., Goodman, J. I., and Kelley, W. E. (1944): *J. Amer. med. Ass.*, **124**, 478.

SKIN DISEASES IN THE TROPICS

BY A. GIRDWOOD FERGUSSON, M.D., F.R.F.P.S.

Assistant Dispensary Physician for Diseases of the Skin, Western Infirmary, Glasgow; Assistant Visiting Physician, Diseases of the Skin, Stobhill Hospital, Glasgow. Formerly Lieut.-Col., R.A.M.C., Adviser in Dermatology, South East Asia Command.

A WIDE diversity of skin conditions occurs in tropical and subtropical regions. Of these diseases, some are indigenous and others common disorders of global distribution which under tropical conditions may assume a new and even serious significance as regards the health of any given community. For the purposes of this article, it is convenient to adopt the following simple classification of cutaneous diseases:—

    (A) Pure dermatoses
    (B) Parasitic and infective diseases
        (1) Diseases due to animal parasites
        (2) Diseases due to vegetable parasites
    (C) Nævi and neoplasms
    (D) Diseases of the appendages

With reference to group A, some further subdivision is necessary, and it may be said that the heading covers:—

    (1) Diseases due to vascular disturbance, e.g. urticaria, erythema multiforme.

    (2) Diseases due to serous exudation, e.g. eczema and dermatitis.

    (3) Diseases characterized by scaling and lichenification, e.g. psoriasis.

    (4) Diseases characterized by dystrophy, atrophy, hypertrophy or pigmentary disorder, e.g. ichthyosis and leucoderma.

DERMATOSES

All the common vascular disorders of the skin are of global incidence and are frequently encountered in the tropics. The most commonly noticed is urticaria.

Urticaria.—It is well known that this condition is a "type reaction" and associated with the group of so-called allergic diseases. In addition, individuals sensitive to certain foods and drugs, such as arsenic, quinine and sulphonamides (Peterkin, 1945), may develop the disease, which may also complicate external skin infestation by animal and vegetable parasites. Etiological factors met with almost solely under tropical conditions are heat and parasitic infestations of the intestines, e.g. tapeworm, ascariasis, ancylostomiasis and amœbiasis.

The symptomatology is familiar, the eruption being intensely itchy and composed of transient wheals of various shapes and sizes. Under tropical conditions the treatment of concurrent parasitic diseases and the avoidance of undue exposure to high temperatures are measures which are often

successful in resistant cases. Locally a simple antipruritic lotion such as the following should be used:—

℞ Menthol .. .. 2 grains (0.13 gm.)
Calamine lotion .. .. .. to 1 ounce (28.4 c.cm.)

Diseases characterized by serous exudation into the skin, such as all types of traumatic and sensitization dermatitis, eczema, herpes simplex and zoster, dermatitis herpetiformis and pemphigus are commonly seen in tropical areas. Secondary pyococcal infection of the original lesions and consequent severity and intractability constitute the main hazards in the tropics. These complications are probably predisposed to by excessive sweating with its relatively alkaline pH, which furnishes a suitable nidus for the proliferation of pyogenic organisms.

There is one disease of this group which is of particular significance in countries in which bright sunlight is usual, namely prurigo æstivalis (Hutchinson, 1878; Adamson, 1906).

Prurigo æstivalis.—This condition chiefly affects young adult and adolescent males and is thought to be due to the visible rays of the solar spectrum in addition to some of shorter wavelength. The nature of the photosensitizing substance is not known, and there is never an associated hæmatoporphyrinuria as in the closely allied condition known as hydroa vacciniforme. In temperate zones the condition appears in summer and subsides in winter. In the tropics it may be an ever present and extremely annoying ailment.

The symptomatology is very definite, the eruption being of papular or papulo-vesicular eczematous nature and involving exposed parts, namely the face, forehead, backs of the hands and forearms and knees. Itching is variable but may be extremely severe, and the lesions heal without scarring unless secondary infection has occurred.

As regards treatment, attempts to desensitize by means of minimal exposures to ultra-violet and luminous rays and non-specific protein therapy have proved unsatisfactory. The patients must avoid undue exposure to sunlight and should use a local protective cream containing quinine, ichthyol or disodium naphthol sulphonate, all of which exert a filtering action upon ultra-violet rays. Against luminous rays the best protective is resorcin, and the following preparation has been suggested for local application (Urbach and Konrad, 1929).

℞ Resorcin .. .. 3 per cent.
Zinc paste .. .. .. to 1 ounce (31.104 gm.)

In some cases the only answer to this problem is removal to a temperate climate, but many clear up spontaneously on reaching adult life.

The common diseases characterized by lichenification and scaling met with in the tropics are psoriasis and seborrhœic dermatitis in its various forms. The effects of tropical climatic conditions upon the response to treatment of these disorders forms an interesting and important study. A dermatosis resembling both lupus erythematosus and lichen planus has occurred among allied troops in the Mediterranean and Far Eastern areas

during the late war, but cases have been few and the etiology is still in doubt.

Psoriasis.—This is an essentially relapsing disease appearing typically at more or less regular intervals with intervening periods of complete or almost complete involution. The erythematous eruption with its characteristic dry silvery scaling and its tendency to involve the scalp and extensor joint surfaces, is well known.

One of the most popular theories as to etiology has long been that of light deficiency. This is based upon the facts that the disease accounts for 8 per cent. of all skin disorders in a country such as Iceland, and only 1 per cent. in the southern United States, that relapses tend to occur in cold seasons, and that the eruption is distributed mainly on covered parts of the body.

This theory has, however, not completely answered the problem of etiology, and in tropical areas any benefit derived from sunlight, so often extraordinarily effective in temperate climates, is usually more than offset by the deleterious results of excessive sweating and secondary pyogenic infection. Further, the disease appears to be quite common among the scantily clothed natives of tropical regions.

Treatment follows the lines usual in temperate regions, save that, owing to the macerating effect of greasy ointments and creams under tropical conditions, paints and lotions are more used locally. The acute case is best treated locally by means of sulphur in emulsified form (2 per cent.) and the chronic with tar or modified chrysarobin (cignolin) in the form of a paint. Crude gasworks tar is less irritant than pine or juniper tar, and is often used in undiluted form or made up as the following paint :—

℞ Crude coal tar	..	..	..	20 per cent.	
Acetone	..	..	..	..	to 1 ounce (28.4 c.cm.)

Cignolin is used likewise in strengths of $\frac{1}{2}$ to 2 per cent. Tar and ultra-violet light baths, given twice or thrice weekly, are often extremely helpful in resistant cases.

Seborrhœic dermatitis and seborrhœides.—This group of diseases includes seborrhœic eczema, acne vulgaris and rosacea. The importance attached to such conditions in tropical areas is due to the fact that secondary infection by pyococci tends to prolong their course and lead to marked chronicity, whilst tropical sunlight has a deleterious effect, particularly as regards rosacea.

As regards etiology, the seborrhœic diseases are still thought by many clinicians to be basically due to infection of the skin by organisms which normally exist as saprophytes upon the scalp, and which are at times rendered pathogenic by the existence in the tissues of the subject of certain conditions as yet not fully understood. The organisms are (a) the pityrosporon of Malassez (a yeast), (b) staphylococcus epidermidis albus, and (c) the acne bacillus. In the more eczematous forms of the disease there is superadded infection by pyogenic organisms, and copious sweating and lack of elementary hygiene are important aggravating factors, the latter more particularly among native peoples.

The symptomatology varies considerably with the different types and stages of the disease. The three main types are (a) a circinate, erythematous and squamous process, the scaling being of greasy consistency and the erythema of a tawny hue, whilst the sites of election are the sternal and interscapular regions; (b) a more acutely eczematous eruption characteristically involving hair-bearing areas and the body flexures, a type of folliculitis (sycosiform seborrhœa) being a common associated finding, and (c) the acneiform eruptions, vulgaris and rosacea.

As regards treatment, a common impression that seborrhœic conditions, particularly acne vulgaris, improve in tropical climates owing to the beneficial effects of ultra-violet light must here be dispelled. Any benefit so accruing is usually, as in the case of psoriasis, more then offset by the deleterious effects of sweating, as sweat absorbs ultra-violet rays (Crew and Whittle, 1938).

It is therefore obvious that seborrhœic subjects are "bad risks" in the tropics, and that they should spend as much time as possible in dry and cool areas where some benefit from natural sunlight may be expected (e.g. hill stations). Curative treatment is best carried out under hill conditions, and follows the lines usual in temperate zones. Sulphur is the local therapeutic "sheet anchor," and is usually employed in lotion form to avoid maceration of the skin. The original nidus of infection, the hairy scalp, must receive careful attention; the hair must be trimmed short or cropped and the head shampooed daily with soap spirit. Diet should be bland in acute cases. In severe secondarily infected cases I have found that parenteral penicillin in dosage of 15,000 units every three hours, up to a total of 120,000 units, quickly clears the superimposed sepsis. Ultra-violet light baths and X-ray therapy have their uses in acne vulgaris and chronic patchy seborrhœic eczema.

Of the atrophies, hypertrophies, dystrophies and pigmentary disorders of the skin, the most important in the tropics are ichthyosis, phrynoderma, leucoderma and ainhum.

Ichthyosis congenita.—This condition is a congenital hypertrophy of the skin, usually of generalized nature, which in some cases may be associated with thyroid dysfunction. It is often familial and hereditary. There is a tendency in temperate climates for the disease to grow worse in cold weather, and mild cases may improve in the tropics. The severe case, however, is usually worse in warm climates.

There is generalized thickening of the skin and diminution or absence of sweat and sebaceous secretion. It is in view of this glandular inactivity that the severe case tends to ·develop symptoms of heat exhaustion in tropical regions, the skin remaining unaffected. A few milder examples, however, may actually benefit by the over-stimulation of their remaining glands by hot atmospheres. From the point of view of the dermatologist, treatment can only be palliative, but small doses of thyroid, daily tepid baths and a local ointment such as the following may be of considerable help, provided that the patient can be kept in a cool atmosphere.

℞ Salicylic acid   ..   ..   ..   5 grains (0.32 gm.)
  Solution of coal tar   ..   ..   5 minims (0.3 c.cm.)
  Lanoline ..   ..   to 1 ounce (31.104 gm.)

Phrynoderma.—This disorder is thought to be chiefly due to avitaminosis A, although a recent worker has cast some doubt on this (Stannus, 1945). It is common in the tropics, and this may be due, apart from faulty dietetics, to the incidence of such bowel diseases as sprue and hill diarrhœa, in which there is diminished absorption of fat and therefore of fat-soluble vitamins.

The skin eruption consists of dry spiny follicular papules of small size, with associated fine scaling and brown pigmentation. The sites of election are the extensor limb surfaces and the nape of the neck and shoulders, but in severe cases the face, flanks and buttocks may be involved. Symptoms and signs of an associated bowel disease are of course often present, or there may be a history of malnutrition with other evidence thereof.

Treatment must obviously be directed towards eradication of any concomitant disease or the building up of an adequate diet. Vitamins are given in addition, and the local treatment usually takes the form of a bland greasy application containing a keratolytic substance, such as salicylic acid.

Leucoderma.—The etiology of this condition is, in its acquired and non-specific form, unknown, The symptomatology appears to depend upon exhaustion of the pigment-forming power of certain cells in the corium and basal epidermic layer, and the eruption takes the form of de-pigmented patches of various sizes and irregular distribution, which do not give rise, except in a minority of cases in the tropics, to any subjective disturbances or objective signs. In fair-skinned persons in the tropics, however, there is occasionally considerable vesicular reaction to sunlight in the pale areas. There may also be some psychological upset due to ignorance of the nature of the disease among native populations, by whom it is often wrongly supposed to be the neural type of leprosy.

As regards treatment, cure is doubtful, although some cases heal spontaneously. Reassurance with regard to the possibility of leprosy is very important when dealing with native patients. Good cosmetic effects may be obtained by staining the white areas with walnut juice, and in some cases re-pigmentation may be induced by sensitization of the skin of the patch by application of a photodynamic substance, such as oil of bergamot, followed by graduated exposures to a source of ultra-violet light. In cases hypersensitive to solar rays, use may be made of the resorcin paste mentioned under prurigo æstivalis.

Ainhum.—This is classified as one of the cutaneous atrophies and is essentially a tropical disease, the few cases which have been reported in the United States having occurred mainly among negroes. In the tropics, negroes are, in most instances, the victims. The bulk of the evidence now available points to the condition being a tropho-neurosis.

Ainhum is a disease of the hands and feet which is characterized by linear strangulation and ultimately by spontaneous amputation, accompanied by considerable pain, of one or more toes or fingers. The onset is manifested by the development of a narrow groove on the flexor aspect of the first

interphalangeal joint of the affected digit. The part is eventually encircled by a firm cartilaginous ring, the free end of the member becomes swollen and gangrenous and spontaneous amputation occurs. The course of the disease is slow. The treatment of choice is amputation above the encircling ring, and in most cases this is very successful.

PARASITIC AND INFECTIVE DISEASES

Parasitic and infective diseases encountered in tropical regions are in some cases peculiar to those parts of the world, but most occur with equal frequency in temperate zones. As shown in the classification, they may be divided into two main groups.

(1) *DISEASES DUE TO ANIMAL PARASITIC INFESTATION*

Scabies and pediculosis.—These infestations are common in the tropics, particularly among crowded native populations. They follow the usual lines as regards symptomatology, except that swift secondary pyococcal invasion is the rule and treatment must of necessity be speedy and thorough if such complications are to be avoided.

Straw or barley itch.—The arachnid insect known as *Pediculoides ventricosus* is the cause of this disease, which is quite commonly seen in tropical regions. The parasite produces its effects upon the human skin by exudation of an irritant fluid and never burrows. The eruption produced is intensely itchy, often generalized and of papulo-vesicular and secondarily pustular nature. It often closely resembles varicella, but the face is seldom involved. Treatment is simple, antipruritic lotions, as for urticaria, usually sufficing. Occasionally a parasiticide, such as sulphur, is required. It is probably wise to disinfest clothing and bedding.

Copra itch and plum itch.—*Tyroglyphus longior*, a small acarus-like parasite, occurs on cocoanuts and copra and causes an itching eruption in man which is practically indigenous to the tropics. The insect produces its effects as does that of straw itch. The eruption resembles that seen in straw itch, but is localized to the hands and forearms. It usually heals spontaneously on the victim ceasing to handle infected nuts. A similar condition is caused by the *Carpoglyphus passulorum* and occurs among plum and fig labourers (O'Donovan, 1920).

Tungiasis.—The parasite *Rhinochoprian penetrans* (or *Tunga penetrans*) is indigenous to tropical America and Africa. The female flea, when gravid, causes skin damage by burrowing head downwards and anchoring herself in the tissues. Infestation may be multiple, and the lesions, ulcers with dark central plugs, usually occur on the feet and ankles.

Treatment consists in removal of the parasite with a blunt needle and application of a mercurial lotion to the ulcer.

Myiasis.—Worm infestation of the skin is common in the tropics, examples being filariasis, larva migrans and "ground itch".

Larva migrans.—This disease is usually due to burrowing by the larva of the bot-fly (*Gastrophilus*) and almost unbelievable convolutions of a raised and linear nature mark the track of the parasite in the skin. Treatment, by

injection into the lesions of a few drops of chloroform, gives speedy cure.

Cutaneous leishmaniasis.—It is not yet clear whether the nodular eruption affecting the face in treated cases of kala-azar is due to the protozoon *Leishmania donovani* or to the antimonial preparations used in treatment. South American dermal leishmaniasis and oriental sore are, however, undoubtedly due to species of leishmania, probably *Leishmania tropica.* The South American example (espundia) appears to be endemic in the great rubber district of that continent, whilst oriental sore is chiefly seen in tropical and subtropical regions, although occasionally found in Europe. In both forms the lesions chiefly affect exposed areas and in oriental sore the organisms are injected by the bite of a sandfly. The main difference appears to be that in espundia there is a greater tendency to local lymphatic involvement.

Oriental sore takes the form of a hard, raised, button-like process with or without central ulceration, which is painless unless secondarily infected by pyococci. The untreated lesion shows slow spontaneous healing and usually confers complete immunity.

Attempts to hasten the natural healing process have been mainly unsuccessful, although claims have been made for the beneficial effects of a course of parenteral antimony combined with local applications of 2 per cent. tartarated antimonial ointment until a sharp reaction is produced:

(2) *DISEASES DUE TO VEGETABLE PARASITIC INFESTATION*

Diseases due to vegetable parasites are in some instances indigenous to the tropics but the bulk are not so. They may be divided into fungus and bacterial groups.

Fungus diseases of global distribution, such as all types of scalp, body and nail ringworm, favus, tinea versicolor, actinomycosis, blastomycosis and sporotrichosis, are commonly encountered under tropical conditions. They run, in general, a more severe course than in temperate areas and it is worth noting that a condition confined to children in Europe, namely small-spored scalp ringworm, occurs in epidemic form among adult natives, particularly Ghurkas. Mycetoma, almost wholly indigenous to the tropics, is a disease of mainly surgical significance.

Treatment follows usual lines, paints and lotions being used locally. A useful prophylactic measure against eczematoid ringworm of the foot (athlete's foot) is 10 per cent. aqueous solution of sodium hexa-meta-phosphate, applied twice daily. This diminishes excessive sweating and prevents maceration of the skin and the provision of portals of entry for the causal fungus. For body ringworm in the tropics successive paintings with 1 per cent. aqueous solution of silver nitrate and strong tincture of iodine are useful, particularly in the treatment of dark-skinned patients.

Tinea imbricata.—Also known as Tokelau ringworm, this condition is indigenous to tropical areas and is caused by the fungus *Endodermophyton* (*Castellani*). The parasite produces a remarkably itchy eruption in the form of concentric ringed and scaly patches resembling "watered silk" on a dark skin. In treatment the better known fungicides have proved of little use. A

special paint devised by Castellani, which contains 12 to 25 per cent. of resorcin in the ounce (28.4 c.cm.) of compound tincture of benzoin is most effective.

Trichinocardiasis.—This disease is thought by some clinicians to be identical with another, known as leptothrix, which is usually classified under "diseases of the appendages." The causal fungus, *Nocardia tenuis*, may attack either hair or glabrous skin. The disease occurs commonly in the tropics. When hairs are involved, the axillary and crural areas are usually affected. The hairs show irregular "beading" and there is generally an associated red, yellow or black pigmentation of doubtful origin. As regards the type in which the skin is affected, the lesions produced are ulcerative, granulomatous swellings and any part of the body may be involved. Ordinary fungicides are quite useful in treatment.

Piedra and pinta.—Piedra, a tropical disease affecting the scalp hair, and pinta a disease affecting both scalp and glabrous skin which is common in South America and Ceylon, fall into this group. Both are thought to be due to several forms of fungus acting concurrently, including trichophyta and monilia, and both respond well to ordinary parasiticides, particularly mercurials.

Bacterial diseases most commonly encountered in the tropics include ecthyma, tropical ulcer, leprosy and framboesia (yaws). The two last are problems of the leprologist and general physician respectively.

Ecthyma.—This condition is due to infection of the skin by pyococci and occurs with equal frequency in temperate and tropical areas, usually as a complication of animal parasitic disease. During the late war a number of confusing synonyms, such as desert and jungle sore, have been applied to this simple disorder, thus tending to cause its identification with more severe conditions peculiar to the tropics. Claims have been made that in tropical climates the condition is often a manifestation of cutaneous diphtheria, but such cases have usually been found in association with epidemics of faucial and nasal diphtheria, and the general opinion would appear to be that infection of lesions already present occurs *post hoc*.

Arising usually as a complication of a previous itching skin disease, single or multiple ulcers appear, the limbs being the parts chiefly involved. The lesions have irregular edges, little or no infiltration of their bases and central dark crusts.

As regards treatment, any concomitant parasitic disease must first be dealt with, and if diphtheria bacilli are seen in direct smears from the lesions, serum must be given in full doses. Prophylactic local measures include prompt antisepsis in the case of all minor abrasions, and in the presence of established disease the modern therapy of choice is penicillin in normal saline as a spray three hourly (500 units per c.cm.).

Tropical ulcer.—The causal organisms are here thought to be the spirillum and fusiform bacillus of Vincent. The condition is common in Africa, and the sores occurring among the Naga tribesmen of South-Eastern Assam are almost certainly of the same type. A sloughing phagedænic process is pro-

injection into the lesions of a few drops of chloroform, gives speedy cure.

Cutaneous leishmaniasis.—It is not yet clear whether the nodular eruption affecting the face in treated cases of kala-azar is due to the protozoon *Leishmania donovani* or to the antimonial preparations used in treatment. South American dermal leishmaniasis and oriental sore are, however, undoubtedly due to species of leishmania, probably *Leishmania tropica*. The South American example (espundia) appears to be endemic in the great rubber district of that continent, whilst oriental sore is chiefly seen in tropical and subtropical regions, although occasionally found in Europe. In both forms the lesions chiefly affect exposed areas and in oriental sore the organisms are injected by the bite of a sandfly. The main difference appears to be that in espundia there is a greater tendency to local lymphatic involvement.

Oriental sore takes the form of a hard, raised, button-like process with or without central ulceration, which is painless unless secondarily infected by pyococci. The untreated lesion shows slow spontaneous healing and usually confers complete immunity.

Attempts to hasten the natural healing process have been mainly un-successful, although claims have been made for the beneficial effects of a course of parenteral antimony combined with local applications of 2 per cent. tartarated antimonial ointment until a sharp reaction is produced:

(2) DISEASES DUE TO VEGETABLE PARASITIC INFESTATION

Diseases due to vegetable parasites are in some instances indigenous to the tropics but the bulk are not so. They may be divided into fungus and bacterial groups.

Fungus diseases of global distribution, such as all types of scalp, body and nail ringworm, favus, tinea versicolor, actinomycosis, blastomycosis and sporotrichosis, are commonly encountered under tropical conditions. They run, in general, a more severe course than in temperate areas and it is worth noting that a condition confined to children in Europe, namely small-spored scalp ringworm, occurs in epidemic form among adult natives, particularly Ghurkas. Mycetoma, almost wholly indigenous to the tropics, is a disease of mainly surgical significance.

Treatment follows usual lines, paints and lotions being used locally. A useful prophylactic measure against eczematoid ringworm of the foot (athlete's foot) is 10 per cent. aqueous solution of sodium hexa-meta-phosphate, applied twice daily. This diminishes excessive sweating and prevents maceration of the skin and the provision of portals of entry for the causal fungus. For body ringworm in the tropics successive paintings with 1 per cent. aqueous solution of silver nitrate and strong tincture of iodine are useful, particularly in the treatment of dark-skinned patients.

Tinea imbricata.—Also known as Tokelau ringworm, this condition is indigenous to tropical areas and is caused by the fungus *Endodermophyton* (*Castellani*). The parasite produces a remarkably itchy eruption in the form of concentric ringed and scaly patches resembling "watered silk" on a dark skin. In treatment the better known fungicides have proved of little use. A

SOCIAL MEDICINE IN THE TROPICS

By W. H. KAUNTZE, C.M.G., M.B.E., M.D., F.R.C.P., D.P.H.

Medical Adviser to the Secretary of State for the Colonies.

FOR those who have never lived in the territories which form the Colonial Empire it is difficult to visualize the vast difference which exists between the social conditions of Britain and of these countries, most of which lie in the tropical zone. This difference is contributed to by the general lack of education, a poor social economy and a lassitude, partly attributable to the sapping of human energy by the ravages of endemic disease.

In many places in the tropics, society consists of a comparatively small number of educated or semi-educated men and women and a majority of illiterate or semi-literate people. Warning is always being given about the unrestricted growth of populations in countries dependent primarily upon agriculture; indeed, in some places, such as Barbadoes, the population is already outstripping the carrying power of the land. The matter which should cause more concern, however, is that it is the illiterate and poorest section of the population which is growing most rapidly and increasing just those classes which cause an economic and social problem. A vicious circle is created, and until it can be broken in some way the problem can only get worse.

STANDARD OF LIVING

In most of these countries of the Colonial Empire the general standard of living is low. Dwellings are, by our standards, poorly constructed, although it must be remembered that in the tropics huts are used more as bedrooms than living rooms, household activities commonly being carried out in the open air under trees. Not only are the houses poorly built, but they are usually poorly maintained and for this reason soon become dilapidated, whilst in the more backward areas they lack light and ventilation and privacy, and at night are often uncomfortably crowded.

It is, however, in the urban areas that the *overcrowding* problem is at its worst. In rural areas, the family can usually manage to build for themselves accommodation of sorts sufficiently commodious for their needs (this is not entirely true where revenue is collected by a hut tax, a very effective deterrent to over-building). In the towns this is impossible, and the country-man with his family who has come to the town to find work must accept whatever lodging he can get. Since accommodation is always insufficient to meet demands, the lodging is usually at best a room, and may even descend to the sharing of a room with other families. In one town, latrines in back-yards were rented out to eager tenants for sleeping quarters during a period when high wages for new constructional work drew many labourers from the country.

duced. Many neglected cases may actually suffer limb loss, owing to the extensive ulceration.

In treatment, neoarsphenamine, in small doses of 0.15 gm. twice weekly, combined with local treatment, as in ecthyma, is often very effective in early cases. More extensive processes usually require surgery.

NÆVI AND NEOPLASMS

Nævi and neoplasms of the skin are never peculiar to tropical regions, although congenital leucoderma (albinismus) is probably more frequently found in coloured races, largely as a result of consanguinity. A warty condition (verruga peruana), indigenous to lower Peru, is actually a specific infective exanthem.

DISEASES OF THE APPENDAGES

Diseases of the appendages have already been largely considered, as regards affections of the hair, under parasitic and infective diseases. Diseases of the nails most commonly seen in the tropics are tinea and moniliasis and have also already been mentioned. The sebaceous glands are chiefly involved in seborrhœic states (see p. 116).

The sweat glands are probably the organs most affected by tropical climatic conditions and, apart from simple localized or generalized sweating, one indigenous disease occurs in which they are almost certainly implicated.

Miliaria rubra (prickly heat).—This condition is confined to tropical climates and more particularly to those in which humidity is great. Obese and hyperidrotic persons are usually severely affected, but nearly every individual in the tropics is a sufferer. A fiery red papular eruption, accompanied by an intense prickling sensation, affects the skin of the entire body in severe cases, although that of the face, hands and feet is relatively seldom involved. Secondary pyogenic infection produces a bullous impetigo which is known as "tropical pemphigus", and secondary eczematization is also frequent in neglected cases. In treating the disease, emphasis should be laid upon the avoidance of unnecessary exertion, stimulant foods and alcohol. The clothing should be light, and a tepid bath should be taken twice daily, followed by copious application of the following dusting powder (Lew 1942):—

℞ Flowers of sulphur
  Boracic acid
  Zinc oxide powder
  Starch powder āā p.a.

References

Adamson, H. G. (1906): *Brit. J. Derm.*, **18**, 125.

Crew, W. H., and Whittle, C. H. (1938): *J. Physiol.*, **93**, 335.

Hutchinson, J. (1878): "Lectures on Clinical Surgery", London, **1**, 126.

Lewis, R. R. (1942): *J. roy. Army med. Cps.*, **78**, 86.

O'Donovan, W. J. (1920): *Brit. J. Derm.*, **32**, 297.

Peterkin, G. A. G. (1945): *Brit. med. J.*, **ii**, 1.

Stannus, H. S. (1945): *Proc. roy. Soc. Med.*, **38**, 337.

Urbach, E., and Konrad, J. (1929): *Strahlentherapie*, **32**, 193.

the sombre picture drawn above of health conditions in tropical territories. That more has not been done to eliminate such diseases is due to several factors. In the first place medical services in Colonial territories arose originally from the provision of medical officers to serve the needs of the immigrant European population, which was largely composed of Government servants and traders. Medical services were gradually extended to include the provision of treatment for the indigenous population in the neighbourhood of European settlements, and as the opening up of the Colonies proceeded, so medical treatment was gradually extended farther afield. As a result of this development, the emphasis during the earlier periods of Colonial settlement was laid on curative work. Indeed, it may be said that in those days so little was known of the cause and prevention of tropical disease that elimination of it could hardly have been attempted. It was only in 1897 that Ross discovered the transmission of malaria by the mosquito. Thus it is only in this century that the new knowledge of tropical diseases as applied to their prevention is clearly seen.

Another factor which has worked against the attempt to eliminate community-wide disease has been the undue emphasis in the current system of medical education on the cure of disease rather than on the elimination of the factors which cause it. The large number of sick seeking medical treatment in Colonial territories has whetted the laudable desire of medical men serving in these countries, to relieve suffering rather to the exclusion of attempts to reduce the causes of it. In recent years, the emphasis on prevention has been gradually growing, for the modern outlook on the problem of sickness is different from that of our forefathers. No longer is it sufficient to struggle to make the sick well; the aim now is to promote good health and to eliminate preventable disease. A standard no less high must be the aim in Colonial territories, where so much of the community-wide disease is preventable and knowledge of the causation of tropical disease has grown so greatly that it is now possible largely to eliminate it. But this can be done only if adequate staff is provided and adequate funds given to carry out the measures, many of them expensive, which are essential. There is one other obstacle to overcome, and that is the reaction of the peoples themselves, for it is common knowledge that the populace in Colonial territories is either intensely suspicious of new ideas or so apathetic, as the result of poverty and disease, as to have no desire to change its condition. So, if community-wide disease is to be tackled, the confidence of the population must first be secured and their whole-hearted cooperation in the measures for their welfare enlisted, because it is only when they realize that they are responsible for their own good health that measures taken to eliminate disease can ever have any permanent effect.

Attack on preventable disease has been attempted in different ways in the past. One method which has been favoured has been the organization of a campaign to stamp out a particular disease. This method has had three

Water supply and sanitation provide further problems. Except in large towns where there may be a pipe-borne supply, the peasant is dependent upon rivers, springs and wells for his water, none of which is purified although in most cases heavily contaminated. Moreover, it has often to be carried by hand for long distances, particularly in those places where the people do not live in villages but on small holdings. In such circumstances bathing and laundering are usually carried out at the river or well side, a potent cause of pollution.

Sanitation is also primitive, if indeed existent at all. In many villages the bush or jungle serves as the privy. Soiling of the ground spreads such diseases as ancylostomiasis, whilst the tropical rain washes bacterial infection from the soiled land into the nearby water supply. Where pit latrines have been provided, they are as often as not unused because of taboos and similar superstitions. It is perhaps fortunate that the air temperature in the tropics is so high and thus excrement dries rapidly. Nevertheless, helminth eggs have great powers of resistance, and drying of excrement produces dust which wind and flies disperse with its quota of helminth eggs and bacteria.

Diet.—So many of the amenities which in civilized life are considered essential for health, are lacking in these more primitive communities. To this must often be added ignorance of the best foods to grow and the best ways of cooking them. Experience and lore handed down orally for generations have shown the peasant which crop can be most easily grown and which is the least likely to suffer in seasons when there is drought or excessive rain. But it does not follow that the food crop grown to meet these conditions is the most suitable the farmer can produce. It often is not. Too frequently it is starchy and ill-balanced as a diet, and although to a casual glance the countryman looks well nourished, a closer examination often reveals signs of nutritional deficiency.

DIFFICULTIES OF DISEASE PROPHYLAXIS

Mention has already been made of the prevalence of chronic disease. Much of it is insect-borne, as, for example, such conditions as malaria and trypanosomiasis, whilst some may come from dust or water, or by the intermediary of the housefly, or from the handling of food by infected persons. Lowered vitality, arising from poor nutrition, may well be a factor of importance in inducing chronic disease and enhancing its effects in these less developed territories.

In the tropics, prevalent diseases may be divided into two groups: (1) those which are almost community-wide and (2) those which are confined to individuals here and there. In countries where medical work has been carried on for many years, such as Great Britain, the first group is practically non-existent, thanks to the preventive medical services. This is not so in the tropics, and the existence of community-wide diseases largely colours

secure the cooperation of the inhabitants of the area in which the team is working. It is therefore essential to choose for the initial venture a locality where there are leading citizens genuinely wishful to improve the condition of themselves and their neighbours. Before the actual work begins, the possibilities of disease control must be expounded to these men in such a way that they not only grasp the plan of the work, but become urgent in demanding that a start should be made in controlling disease in and about their own homes. The idea of self-responsibility must be driven home and the active cooperation of the people in carrying out and maintaining the measures required for disease control obtained. Each man, woman and child in the village must feel himself, or herself, personally responsible for taking an active part in the undertaking and for the maintenance of control measures after the team has left. This will be rendered easier if, from the start, the assistance of a village health committee, elected by the people, is secured.

It is impossible to describe here the actual work which will be required in all places but, generally speaking, the main measures will be the provision and protection of water supplies; adequate provision for conservancy and refuse disposal; measures against disease-carrying insects; improvement of houses and prevention of overcrowding; improved agricultural methods; growing of the right food crops; and so on.

Methods of control.—In this campaign against preventable disease, the team will have to keep clearly in mind what it has to do if it is to complete its task within a reasonable period; there are certain diseases, for example yaws, in which sufferers can be made non-infective to others in a comparatively short period of time, yet to free them completely from the disease may require treatment over many years. The rendering of such patients non-infective is sufficient for the purposes of the team, who should clearly understand that the treatment to completion of cases must be left to the local district staff. To the medical man brought up to think of the treatment of individual patients, this may seem a hard demand, but when the first aim must be to rid the coming generation of the risks its fathers had to meet, medical effort must be expended in the way which will most benefit the community and not the individual. That it is possible to work on these lines is indicated by experience in one Colonial territory where, in the early twenties, a certain clinic dealt with over one thousand cases of yaws a week; to-day it is extremely difficult to find a case anywhere in that district, yet no-one pretends that the cases treated originally in the clinic were completely cured.

Staff required.—With the great mass of preventable community-wide disease removed, the medical staff left behind in the area after the special team has moved on will be able to tackle the task posed by those diseases which for the most part attack individuals in the community. Some of these diseases have a known causation which can be removed; about others little is as yet known, although it is known that many of them when fully

defects which have often rendered results negligible. In the first place, the people were passive agents in the campaign, rarely understanding what it was all about and perhaps a little resentful at the work they were forced to do for their own good. In the second place it took no account of the fact that whereas one disease might be an important and widespread factor in ill health, other factors existed which remained untouched. Results were therefore often much less remarkable than had been anticipated. In the third place, whilst money and effort were expended upon the campaign, arrangements for the maintenance of the work done were neglected. Thus, for example, some campaigns of the past against ancylostomiasis have to-day their memorials in the stark remnants of latrines, mostly unused, still studding the countryside. The campaigns were never adequately followed up, and like all regulations impressed from the top had no permanent effect on the lives of the inhabitants. It is sad to think of so much effort and money being wasted.

Another method of attack that has been used left the contest against preventable disease largely to the regular staff of the district. Had this staff been adequate for the task, and had a suitable plan been followed, this method, in association with better propaganda measures, might have proved successful. But in no place in Colonial territories has it been possible to provide medical personnel adequate to combat the widespread preventable disease engulfing the population. What medical staff there was, has been overwhelmed by the immensity of its task and has usually either succumbed to the temptation of concentrating on treatment of the sick or, alternatively, decided to tackle one disease at a time. In most cases, even for this, the staff was insufficient, and no effective result was obtained.

A CAMPAIGN AGAINST DISEASE

A more promising method recently suggested is really a combination of the two just mentioned. An area would be selected for cleaning up by a special team, the size of the area depending upon the staff which could be allocated. The team would absorb, for the time being, all the regular medical staff of the area in which it was working. It would attack preventable disease and at the same time train the local medical staff in the way this could be excluded for the future. When the area had been cleaned up, the team would move on to a new area, leaving the local district staff, now trained in the new methods, to maintain what had been done and to cope with those diseases which attack individuals rather than the community. The difficulty with this method really lies in making a start. Once an area has been cleaned up successfully, there will inevitably come a call from the people in surrounding districts demanding similar action in their own neighbourhood. Therefore too great care cannot be taken to secure members for the first team who have the necessary enthusiasm and the right outlook to carry the initial project to a successful conclusion. One of the important features of this method is to

influence which will be largely instrumental in explaining what is being done and in enlisting the support of the general population in health measures. After the special team has left the area, it will be upon the shoulders of the community nurse and the family doctor that the maintenance of health in the community will depend. For these reasons, too much emphasis cannot be placed both on the selection and the training of men and women to fill these posts. Individuals of character and personality are required if they are to take their place as leaders of the community in the fight for health. Their training must equip them with all the knowledge available for the prevention and treatment of disease, both from the physical and mental point of view. Too little attention in the past has been paid to the influence of the family surroundings and contacts on the health of members of the family, and this aspect must receive due consideration during the training period. As has already been mentioned, a suggested curriculum for the training of community nurses is contained in the Rushcliffe Report on the Training of Nurses for the Colonies (Command Paper No. 6672). I would make one special point in regard to the training of doctors. It is imperative that if such practitioners are to look at their task in the Colonies from the right point of view, they must be imbued with the preventive idea before coming into contact with patients, that is to say, they must be instructed in the principles of social medicine and hygiene, even when studying anatomy and physiology, and this instruction in social medicine should thenceforth continue throughout the remainder of the curriculum. One particular aspect that might be noted is the need for teaching medical students first, that it is the work of the general practitioner and not of the specialist which is the foundation upon which the prevention of disease is based, and secondly, that a patient's illness is acquired in a particular environment, and that when he returns to it on discharge from hospital a recurrence of disease is probable unless some change is made in that environment, or unless he can be taught while in hospital how to adapt himself better to his home or working conditions.

PERSONNEL

In conclusion a word must be said about other medical staff in Colonial territories who aid in the fight against disease. These range from medical practitioners down to the peon employed as an oiler in an anti-mosquito gang. Their skills are as varied as the duties required of them. Some practitioners have been trained in the medical schools of this country, or in those of the Dominion universities; others have been educated in the medical schools of the Colonial Empire, the diplomas of only some of which have been recognized for registration by the General Medical Council here. In general, the training they receive follows that given in this country, with modifications of a minor character to meet special local conditions. A special class of personnel has been developed in some Colonies known as a "medical

developed cause much permanent impairment of health, but if detected and treated early enough leave no permanent ill-effects. In many of these diseases the onset is insidious and may perhaps go unremarked by relatives until too late. For their detection in the earliest stages the skilled eye of doctor or nurse is requisite. As already mentioned, doctors are scarce in most tropical countries, so reliance must be placed on the nurse who, to fulfill this function, must have had special training additional to that required for State Registration. We have called such a nurse a "community nurse," and the type of training she should receive is described in the Report on the Training of Nurses for the Colonies, issued by the Committee presided over by Lord Rushcliffe (Command Paper No. 6672). Provided she has not too many families to look after (500 is suggested as an outside figure, so that she can visit all at fairly frequent intervals), she should be able to detect the first departures from normal physiology or behaviour in her charges. If she is to be the detector of disease, she must have someone to whom she can refer her sick for final diagnosis and advice as to treatment, so she should work within reach of a doctor. For such work the well-trained general practitioner is essential, for he too must have intimate knowledge of the families he serves so that he may know the norm of each individual, although he need not have such frequent contact as the nurse must have.

Preventive measures.—But the district staff of community nurses and medical practitioner can do more than detect the early onset of disease. They can take steps to prevent disease by teaching the value of, and offering, prophylactic inoculation for smallpox, yellow fever, and diphtheria. Even more important can be the measures they take to maintain the health of those who are well. Experience in the Colonies has proved it best to start these preventive services by the establishment of antenatal clinics at suitable places so as to give the unborn infant the best chance in life. These would be held by the community nurse and the midwife, and attended at regular intervals by the doctor. Then provision should be made for maternity services, followed by the institution of infant welfare clinics, nursery school clinics, school clinics and industrial clinics, so that all through life the individual would be cared for and advised how to maintain health. In their visits to homes, the community nurse and medical practitioner would carry on propaganda directed against any conditions in the home which were inimical to health. Their advice is the more likely to be accepted, because, being the two members of the medical services who come into close contact with the people in their homes, both in health and sickness, they will be looked upon as friends.

THE SOCIAL ASPECTS

So, the essential factors in the attack on preventable disease in Colonial territories are the family doctor and the community nurse. During the period when the special team is cleaning up community-wide disease, it is their

RHEUMATIC SYMPTOMS IN GENERAL MEDICINE

By Sir ADOLPHE ABRAHAMS, O.B.E., M.D., F.R.C.P.

Physician, Westminster Hospital; Consulting Physician to London County Council Hospitals.

IT was at one time stated that with a comprehensive knowledge of syphilis the greater part of surgery would be understood. The physicians, in emulation of this attempt at generalization, represented that typhoid fever was similarly related to medicine. There was in these rather picturesque exaggerations a large kernel of truth, having regard to the protean manifestations of syphilis and the symptomatology, the prolificity of complications, as well as the difficulties in differential diagnosis in the case of enteric fever.

I am tempted to indulge in the same sort of generalization in respect to rheumatism, but for an entirely different reason. Instead of a pathological entity with an established etiology, we are dealing with a term which has not even the merit of a symptomatic convenience (as, for example, headache) but which is a vague description of a variety of sensations or disturbances that may be related to any system of the body. It is no exaggeration to say that the term is usually applied symptomatically to the occurrence of pain of variable severity in every inch of the body, quite literally from the scalp to the sole of the foot, with the exception perhaps of unmistakable acute lesions of an abdominal viscus.

DIFFERENTIAL DIAGNOSIS

The practitioner, who must expect perpetually to encounter the complaint of "rheumatism", must be equally prepared to expect a possible relation to any and every system of the body, notwithstanding the layman's puzzled attitude towards his difficulties. For to the layman "rheumatism" is just rheumatism, cured or at least relieved by a small daily dose of Epsom salts, by the adoption of a freak diet, by carrying a raw potato in the pocket, or wearing a ring of peculiar metal appropriately impregnated. The practitioner's difficulties are enhanced by the converse, that rheumatism in the true sense may present itself in a way quite unrelated to the locomotor system. In children, for example, synovitis may on occasion occur as a feature of rheumatic fever, but more frequently an isolated carditis may be expected rather than any complaint of pain. Chorea is even more familiar, whilst tonsillitis, pleurisy or general ill health may be the only rheumatic manifestations. In certain instances, erythema nodosum may have a rheumatic background, and other dermatological conditions, if rarer, are also recognizable. When the frequency with which the rheumatic toxin attacks the endocardium is considered, no emphasis is necessary upon the importance of recognizing these comparatively unconnected symptoms of rheumatism and the solicitude they demand if a subsequent crippling carditis is to be prevented. It is unnecessary to dwell upon the frequency with

A postgraduate lecture delivered for the Empire Rheumatism Council.

aid" or "hospital assistant". These are men, trained primarily as nurses, who have been given additional instruction in the diagnosis and treatment of the common diseases of the country. They normally take charge of dispensaries and small cottage hospitals, under the general supervision of a District Medical Officer, and bring medical aid to many who cannot be reached regularly by the relatively few practitioners that Colonial territories can afford to employ (there are indeed areas where one doctor has to serve as many as one million people). Community nurses have already been spoken about; there are also, of course, nurses serving in hospitals and health departments, trained according to curricula based on that approved for State Registered Nurses in this country, although in most territories some modification has had to be made to adapt them to the general level of male and female education. In countries where this level is low, the curriculum may not even reach the standard proposed for assistant nurses in this country. There are also midwives and sanitary inspectors, but whilst their share in the campaign for health is essential, to detail their work and training would make this article too long. It suffices to say that in general their work and training follow the lines approved in this country.

Finally, in emphasizing the place which the community nurse must take in the fight against disease in Colonial territories, I would not mislead the reader by any suggestion that there are many of them yet at work. A special school for training them exists in the West Indies, and others have started, or are about to start, in other regions, but few nurses are as yet available compared with the large numbers required. The rapidity with which they can be obtained must depend upon the rate of extension of adequate education.

CONCLUSION

Preventive health work is still in its infancy in Colonial territories. The need for its extension is great, as is the need for new ideas and techniques in its application. The problems are such as to tax the ability and skill of men and women of the highest calibre and attainment. Opportunity calls them to this task.

The cardiovascular system may next be considered. Mistakes are possible in both directions. Disease of the shoulder joints or of the subacromial bursa has been confused with angina pectoris on account of the topography of referred pain. *Per contra*, the subjects of coronary arteriosclerosis have sometimes been regarded as suffering for considerable periods from "rheumatic" lesions. Pain more or less constant in the shoulder region—most commonly the left but often the right—has developed within an interval of three or four months after myocardial infarction and has persisted for several years. Shoulder pain has even preceded coronary thrombosis for as long as twelve months. The sufferer from intermittent claudication is prone to present himself with "rheumatic pains in the legs" when one of the various forms of endarteritis may be responsible.

Turning to *the abdomen*, acute rheumatic pericarditis may cause severe epigastric pain. Lesions of abdominal and pelvic organs are on occasion responsible for backache. Conversely, fibrositis of the abdominal wall may be mistaken for an intra-abdominal lesion.

It is not unknown for the *aurist* to be consulted for pain which is in fact attributable to arthritis of the temporo-mandibular joint.

General diseases may be responsible for arthritis and for widely distributed so-called rheumatic pains. Joint lesions occur in bacillary dysentery and in cerebrospinal fever or meningococcal septicæmia, also in undulant fever. The painful affections of bones in Paget's disease and in secondary carcinomatous metastases have also to be remembered, especially as the primary growth may be far from conspicuous. An opportunity is afforded for a diagnostic *tour de force* when it is observed that a patient complaining of rheumatism in the limbs has œdema of the eyelids and is suffering from trichinosis, a disease rare, it is true, but not unknown in this country.

The aches and pains of myxœdema yield to thyroid therapy and not to antirheumatic remedies, and other endocrine relationships are represented by the influence upon arthritic lesions of menstruation, pregnancy and the menopause.

FIBROSITIS

There remains for consideration the most controversial condition of all that are embraced in the purview of rheumatism—fibrositis. Although this diagnosis is often made erroneously there is still plenty of scope for its acceptance, and almost unlimited scope for speculations upon its nature and etiology.

Copeman has demonstrated the existence of palpable tender nodules which are vascular fatty structures liable to œdema and congestion, so impeding the smooth working of muscles and tendons or herniating through foramina in the fascial investments.

In other cases, myalgia is associated with systemic infections. A sudden crystallization appears to occur as the result of some metabolic disturbance, the site of implication being determined by a comparatively trivial injury.

which such cardiac lesions are discovered in adult life, which must have had a rheumatic origin but in which no history of rheumatism is obtainable if synovitis alone is the criterion.

Reverting again to *acute articular rheumatism*, in children osteomyelitis, scurvy and tuberculous arthritis are problems of differential diagnosis. It is more common to diagnose tuberculosis in the case of an acute rheumatic monarticular lesion of a particularly persistent character than to make a mistake in the opposite direction.

In older subjects, whilst acute rheumatic arthritis may occur especially when the disease has previously appeared in earlier life, more caution is called for in accepting this diagnosis. In addition to tuberculosis, sepsis, gout, gonorrhœa, and acute rheumatoid arthritis are in question. The last-named, still of doubtful etiology, may in certain instances provide reason to suppose that an identity or a close association with rheumatic fever may be presumed.

The relationship of sepsis to rheumatism in general is a perpetual source of controversy. Sepsis as a causal factor has been so greatly exaggerated that a disposition towards its complete rejection has followed, but there is abundant evidence to indicate its direct relationship in many instances, and its aggravating influence in more. It is in all probability the secondary microbic invaders which follow upon a gonococcal infection that play the major part in subacute or chronic arthritis, although in the acute stage the gonococcus itself may be incriminated. A frank podagra ought not to be overlooked, but the possibility of less obvious gouty conditions may present considerable difficulty in diagnosis.

The general practitioner may be consulted for "rheumatism" by a patient whose lesion is referable to the *central nervous system*. A good example is afforded by the lightning pains of tabes in which the complaint of rheumatism is sustained by the aggravation afforded by cold wet weather. Although pain is not a symptom, a Charcot's joint is another form of "rheumatic" presentation. Rheumatism in the neck may be referred pain from disease in the cervical spine, whilst malignant metastases in any part of the vertebral column may lead to pain of appropriate distribution.

Less frequently, difficulties of locomotion, vaguely regarded as "rheumatic" are identifiable as a feature of disseminated sclerosis. The converse is equally pertinent; a patient referred to the neurologist as the victim of progressive muscular atrophy (the Aran Duchenne type) because of wasting of the small muscles of the hand or of the shoulder girdle, may be suffering from rheumatoid arthritis with trophic changes. Syringomyelia and cervical ribs have been mistakenly diagnosed in similar circumstances. Chronic headache so severe as to suggest an intracranial lesion, or at least severe migraine, may be of rheumatic origin, affecting the appropriate myofascial tissues. And whilst the recognition of a peripheral neuritis is a legitimate neurological diagnosis, identification of alcohol or diabetes as the cause relegates it to the domain of the general physician.

"MUSHROOM" POISONING

By C. ALLAN BIRCH, M.D., F.R.C.P.

Physician, Chase Farm Hospital, Enfield.

DURING the last three years two small children have died from "mushroom" poisoning* at Chase Farm Hospital. The complete ignorance of most of my colleagues and myself as to possible treatment for such patients has prompted me to record their stories and to summarize the rather inaccessible information on the subject.

CASE REPORTS

Barbara A., aged six years, ate "mushrooms" on Saturday morning, August 18, 1945. She was quite well until the evening, when she began to vomit. Next day she had diarrhœa. On Tuesday, August 21, she was brought to hospital in a comatose condition and died in the receiving room, in spite of atropine, nikethamide, gastric lavage and artificial respiration. At autopsy there was marked liver destruction (weight 17 ounces). Petechial hæmorrhages were present on the intestine and pericardium. Spores of *Amanita phalloides* were found in the intestine. The child's aunt was mildly affected but recovered.

Maureen Y., aged five years, ate "mushrooms" on Saturday morning, August 22, 1942. They had been picked in the fields near Ipswich. She was well until the next morning when vomiting and diarrhœa began. She quickly became delirious and was brought to hospital in a comatose condition on August 24, and died in the receiving room. At autopsy the chief finding was a large and intensely fatty liver. Spores were not sought, so that although *Amanita phalloides* poisoning was highly probable it was not proved.

Mrs. A.Y., aged fifty-four, mother of the above, ate "mushrooms" at the same time. Vomiting began the same evening and continued all night. Diarrhœa started the next day. She was admitted to hospital two days later and quickly recovered. Considerable tenderness was found in the right hypochondrium. A diffuse erythematous rash was present. Rapid recovery as in this case is distinctly unusual.

INCIDENCE

The Registrar General's records show that only 38 fatal cases of fungus poisoning occurred in England and Wales between the years 1920 and 1945. On the Continent, however, they are much more common, and as many as 200 cases are said to occur in Germany every year. The rarity of "mushroom" poisoning is one of its dangerous features, since the hazards are easily forgotten.

POISONOUS FUNGI

Some 2,000 of the larger fungi grow in England. Of these at least as many as 200 are edible but only about a dozen are classed as poisonous and many of these are merely indigestible. It might seem desirable to learn to recognize all the edible fungi at sight, but this is too much to expect. The alternative is to be able to recognize with certainty those which are definitely poisonous and a few which are definitely edible.

---

*The condition is sometimes referred to as "mycetismus" from the Greek mūkēs—a fungus or toadstool, but as few people know the word there is little point in using it.

Although proof is not always forthcoming, there is good reason to suppose that a toxic focus is a crucial factor.

In other instances myalgia is explained as muscular spasm resulting from developmental or occupational deformities, or from postural defects with strain of ligaments and muscle insertions. At the present time the stage is held by the somewhat startling explanation that the large majority of instances of recurrent backache and sciatica are attributable to protrusion of an intervertebral disc causing tension on the posterior longitudinal ligament which is liberally supplied with nerve fibres, or pressure upon nerve roots. Doubtless every one of these explanations is adequate for some cases but not any one for all.

THE PSYCHOSOMATIC ASPECT

A final word must be left to the psychiatrist, or rather to the consideration of rheumatism as a psychosomatic problem. Pleurodynia may represent a fear of pulmonary tuberculosis or of heart disease, and headache the fear of a cerebral tumour. Emotional disturbances are responsible for the outward manifestations of inner emotional tensions that have been provoked by disturbing external events or generated through the accumulation of internal conflicts. The symptoms of feeling sore are interpreted as the consequence of being sore about something, and stiffness as the indication of frustration, of unbending pride or an inability to lower oneself to a certain course of action. In certain circumstances the subject both literally and figuratively " gets it in the neck". "Sciatica" may be traced to a repressed desire to kick somebody, "brachial neuritis" to indulge in fisticuffs. And when such physical factors as cold or wet are easily and speciously blamed, an explanation is forthcoming of rationalization for the sake of personal or purposive ends whilst the inward feelings are repressed.

Such a symbolic representation may appear fantastic, especially as a universal explanation and without regard to any underlying pathology, but it is generally accepted that the emotional disturbances engendered by environmental burdens—poverty, grief, worry and the like—have a relationship to the onset and exacerbation of rheumatoid arthritis. In the case of myalgia, emotion may have led to muscular spasm and tension or have induced vasomotor changes which bring about localized areas of ischæmia or which lower the threshold of sensitiveness to external physical agents.

CONCLUSION

A recent writer has expressed the view that a diagnosis of "rheumatism" is no longer justified. The sufferer from any such complaint is submitted to a diagnostic team—urologist, cardiologist, neurologist, psychiatrist, social worker, orthopædist—so that ultimately the only condition left for the general physician is acute rheumatism. Surely there is more to be said for the use first and foremost of the general practitioner, who should be in a position to call upon any of his specialist colleagues when he is satisfied that a second opinion is indicated.

feature, since the gills of the edible mushroom are never white. The base of the stem is surrounded by a persistent cup or volva, but this may be missing if the whole fungus is not gathered. The spores are identifiable as white, subgloboid bodies measuring 8-11 μ by 7-9 μ, with a central oil drop.

Several poisonous principles have been recognized, the most important of which is the liver toxin, as it is not destroyed by heat.

Allied species are the "fool's mushroom" (*Amanita verna*) and the "destroying angel" (*Amanita virosa*). They resemble *Amanita phalloides*, but their caps are white and so the danger of confusion with the edible mushroom is greater. Both are rare in England.

Fly agaric (*Amanita muscaria*) (fig. 3), so-called because a decoction of it kills flies, is a large and striking fungus because of its red cap with white patches. Hence it is hardly likely to be eaten by mistake. It does not cause death in healthy people. The symptoms produced are due to an atropine-like alkaloid and resemble alcoholic intoxication; certain Siberian tribes eat it for this effect.

FIG. 2.—The Death Cap (*Amanita phalloides*). Gills white. Volva at base of stem. Cap yellowish green.

(Height 4½"; width of cap 3½"; width of stem ⅝")

Certain fungi called "morels" have a sponge-like top and no gills. *Gyromitra esculenta*, related to the edible morels but with a convoluted chestnut-coloured cap, is eaten on the Continent. Its poison, helvellic acid, is hæmolytic but is dissolved out on boiling. Poisoning only results from eating the raw fungus.

SYMPTOMS OF MUSHROOM POISONING

From the point of view of treatment cases of "mushroom" poisoning may be divided into two groups:—(1) Those with early symptoms; (2) those with delayed symptoms.

Early symptoms.—These are diarrhœa and vomiting and may be caused by many fungi. Even edible fungi if not fresh may cause nausea and vomiting, particularly if eaten by allergic subjects. Sometimes the early symptoms are

Many brilliantly coloured and peculiarly shaped fungi are not poisonous at all, but because they are obviously unlike the edible mushroom they are generally avoided. The term "mushroom" is usually reserved for the edible, umbrella-shaped fungi the others being called "toadstools", but this is only popular usage. To many people the word "fungus" has a sinister sound and it has been suggested, although erroneously, that its origin is from the Latin words *funus* (a funeral) and *ago* (I put in motion).
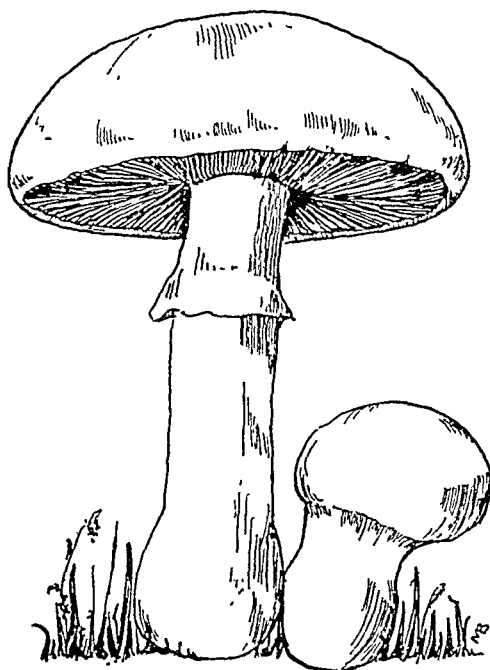
FIG. 1.—Edible Mushroom (*Psalliota campestris*). Gills brownish purple. Base of stem clubbed. No volva.
(Height 3¾"; width of cap 5"; width of stem 1")

It is the custom in this country to eat only the edible mushroom (fig. 1) and to avoid other fungi. But the highly poisonous "death cap" (fig. 2) is easily mistaken by the inexpert for the edible mushroom and herein lies the danger. Dr. Ramsbottom, Keeper of Botany at the British Museum, recommends that "unless this species" (*Amanita phalloides*) "can be recognized with certainty no fungus about which one has no information should be experimented with".

DISTINGUISHING FEATURES .

Most of the popular tests of edibility are fallacious. The edible mushroom peels easily (because its epidermis consists of two layers) but so does the "death cap". Some fungi change colour alarmingly when cut but this does not indicate that they are poisonous. Failure to blacken a silver spoon during cooking is no proof of edibility. The fact that fungi are eaten by rabbits does not mean that they are safe for man. Rabbits can eat the "death cap" with impunity. So it is only by recognizing the poisonous "mushrooms" on sight that poisoning can be avoided. It is not necessary to go into botanical detail concerning the various distinguishing features of the different species. It is important, however, to recognize the "death cap" (*Amanita phalloides*) because this fungus is responsible for from 50 to 90 per cent. of the deaths from "mushroom" poisoning.

The "death cap" (*Amanita phalloides*) (fig. 2).—This fungus has a smooth yellowish green cap. Although this is subject to considerable variation in colour the gills are permanently white. This is an important distinguishing

TREATMENT

Armed with the knowledge that symptoms arising after a meal of "mushrooms" may be followed by death, treatment should be started immediately. The question to be decided is whether or not to treat for "death cap" poisoning. This point may be settled by (1) examining uneaten fungi; (2) considering the time interval between ingestion and symptoms; and (3) examining vomit and fæces for spores. If symptoms appear quickly after ingestion, "death cap" poisoning is unlikely. If the interval is eight hours or more it should be regarded as diagnostic. If in doubt, particularly in a child, treat for the more serious condition.

(1) *Wash out the stomach* and leave in it 2 fluid ounces of white mixture or of a 50 per cent. saturated solution of Epsom salts. Take special care to keep the head lowered if the patient is comatose, so as to avoid inhalation of gastric contents. This treatment will probably be too late in "death cap" poisoning but it would be wise to consider its use in every case.

(2) *Empty the bowel* by enema.

(3) *Give atropine*, 1/50 grain intravenously, to an adult. This is the antidote to muscarine-like alkaloids. Nikethamide, 2 c.cm., may be needed for collapse.

(4) *Treat for liver function failure.* It is the risk of liver damage and not the fact of its presence which should cause treatment to be started. The liver has so many functions at each of which treatment can be directed that no excuse need be made for apparent blunderbuss methods. (a) Glucose: large doses are needed. Hypoglycæmia in hepatectomized dogs can be prevented by injection of glucose at the rate of 0.25 gm. per kgm. per hour. A patient suffering from liver function failure may be compared with a hepatectomized animal and if he weighed 70 kgm. he would need on the basis of 0.25 gm. per kgm. 420 gm. of glucose in twenty-four hours. This should be given by an intravenous drip of dextrose. (b) Insulin aids the deposition of glycogen in the liver and should be given in doses of 10 units for every 50 gm. of glucose given. (c) Calcium: give 10 c.cm. of 10 per cent. calcium gluconate intravenously every four hours. (d) Vitamin B$_1$: give 12,000 units (36 mgm.) daily by injection. (e) Vitamin K: give 10 mgm. daily by injection. (f) Blood transfusion may be used, as it seems to be the most practicable way of increasing the albumin content of the blood, which is low in grave hepatic disease. (g) Methionine and choline: experimental hepatic necrosis can be prevented by an amino-acid—methionine—and fatty infiltration by choline. Although there is as yet no evidence that these substances can reverse established changes it seems reasonable to use them to try to prevent further damage. Methionine is given in doses of 4 gm. and choline chloride in doses of 6 gm. daily, both by intravenous drip. Atropine should not be omitted if choline is used, since it obviates abdominal pain and excessive bronchial secretion due to choline.

(5) *Obtain and administer antiphallinic serum.* Try the Lister Institute,

nervous—delirium and hallucinations—as well as alimentary. *Amanita muscaria* (fly agaric) poisoning is a good example of this.

FIG. 3.—Fly Agaric (*Amanita muscaria*).
Cap red with white patches.
(Height 10″; width of cap 7″; width of stem 1″)

Delayed symptoms come on after a latent period of eight hours or more, and this delay is characteristic of "death cap" (*Amanita phalloides*) poisoning.

Those who have survived its effects say that the "death cap" has a delicious flavour. On the other hand, it has been described as odourless and tasteless. Young specimens are the most poisonous. After an interval of eight to twelve hours, vomiting and diarrhœa, with intense abdominal pain, occur. These symptoms may abate a little, but collapse and death from liver function failure or cholæmia may supervene in at least half the cases.

MUSHROOM POISONING IN FICTION

Fungus poisoning has not been neglected by writers of fiction. *Amanita muscaria* is hardly likely to be eaten by mistake because of its scarlet and white cap, although this may be somewhat washed out by the rain. In "The Documents in the Case", by Dorothy L. Sayers and Robert Eustace, this difficulty is got over by using synthetic muscarine. This was later detected in the organs because it was optically inactive, whereas natural or myco-muscarine is dextrorotatory. There is, however, no record of synthesis of muscarine and also muscarine is detected pharmacologically and not by its optical activity. Such facts as these do not deter the writer of thrillers. Poisonous fungi have been used by other writers, such as Jules Verne, in "A Journey to the Moon", and Sacha Guitry in "Le Roman d'un Tricheur". H. G. Wells, in his story "The Purple Pileus", uses a purple fungus with a muscarine-like effect. *Amanita muscaria* is never purple, however, and he probably chose this colour for its sinister sound.

EARLY RECOGNITION OF DISEASE

VIII.—NON-SPECIFIC ARTHRITIS IN ADULTS

By G. R. P. ALDRED-BROWN, D.M.

Consulting Physician, Royal National Hospital for Rheumatic Diseases, Bath.

THERE are four main diseases within this group—rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, and gout. All four have an unknown or little understood etiology. It is probable that in the first two diseases an infective factor is involved at an early stage, in the third there is a degenerative change due possibly to local vascular involvement, whilst in the fourth there is an error in purin metabolism. These diseases appear to be quite unrelated one to the other, yet on rare occasions they overlap or even seem to merge together.

It may be asked whether or not a differential diagnosis of these forms of arthritis, apart from academic interest, is of therapeutic value. The answer is an emphatic affirmative. Early recognition of rheumatoid arthritis and ankylosing spondylitis can prevent the crippledom of comparatively young patients otherwise condemned to a helpless existence, dying for the life they cannot have, living for the death that will not come. By early diagnosis and sustained treatment the prognosis is reasonably good. In the therapy of these two conditions emphasis should be on the basic principle of early and prolonged rest in the optimum position. Modern technique in plaster splinting has proved of inestimable service in obtaining this position. With the rest, however, there must be the corollorary of active graduated exercises to restore muscle tone. For the one disease gold is a valuable adjuvant, whilst in the other deep irradiation appears to be almost specific. In osteoarthritis the early case can be greatly benefited by an admixture of exercises and rest. In gout, early recognition of an acute phase and the administration of colchicine will produce immediate results; yet, alas, there is little that can be done to avert further attacks. Progression is inexorable in all cases, although in some the rate may be slow.

RHEUMATOID ARTHRITIS

It has been truly said that in this disease the patient's hand is a visiting card. This point cannot be emphasized too strongly. If the hands are affected, then examination of the hands alone is sufficient to make a diagnosis of rheumatoid arthritis. There is nothing vague about the changes; although they may be slight, they are there for all to see and, apart from rare cases of gout which simulate rheumatoid arthritis, there is no other disease which produces such a combination of signs.

EARLY SIGNS.—The earliest changes in *the hands* are three in number and are usually present together: they are fusiform swelling and a dusky tinge of one or more mid-phalangeal joints; swelling of the first two

Chelsea Bridge Road, London, S.W.1. (telephone, SLOane 2181; telegrams, Bacteriology, Knights, London). Failing this source, try Institut Pasteur, 28, Rue du Dr. Roux, Paris XV (telephone, Ségur 01-10). Ask for "Sérum antiphalloidiene". The dose will be indicated on the amount sent. It should be given intravenously with the usual precautions. Air transport can be arranged through British Overseas Airways Corporation, Airways House, London, S.W.1. (telephone, VICtoria 2323; Croydon Airport, telephone, CROydon 4422), or London Office of Air France, 2b, Eccleston Street, London, S.W.1. (telephone, SLOane 0701; Croydon Airport, telephone, CROydon 7744, extension 236).

In case of difficulty in Paris it is suggested that the British Embassy there be approached, at 35 Rue Faubourg Saint Honoré, Paris (telephone, Anjou 2710). It might be quicker to ask the Scientific Office of the French Embassy in London, 1 Carlton Gardens, S.W.1 (telephone, WHItehall 5444) to have the serum sent over by means of the diplomatic bag from le Bourget Airport to Croydon Airport.

(6) Give the *rabbit stomach-brain treatment* of Limousin and Petit. This is based on the fact that whereas cats die after eating *Amanita phalloides* rabbits do not. But the juice of *Amanita phalloides* injected subcutaneously into rabbits is fatal, suggesting that the toxin is destroyed or neutralized in the rabbit's stomach. Cats fed on *Amanita phalloides* plus rabbit's stomach survive for several days. If rabbit's brain is given also, they recover completely. The treatment recommended is to give up to five uncooked rabbits' brains and stomachs minced up daily for several days. Its practicability in a vomiting patient seems questionable but the emergency is so desperate that it should be tried.

All those who have eaten the fungi, irrespective of whether they have symptoms or not, should be subjected to stomach and bowel lavage.

I am indebted to my wife for the drawings and to Dr. John Ramsbottom for much helpful advice. The illustrations are not drawn to scale, and the following are the relative sizes (in inches) :—

	Height	Width of cap	Width of stem
Edible mushroom	3¾	5	1
Death cap ..	4½	3½	⅝
Fly Agaric ..	10	7	1

References

Dubash, J., and Teare, D. (1946): *Brit. med. J.*, i, 45.

Harman, J. B. (1941): *St. Thomas's Hosp. Gaz.*, 39, 151.

Hoechstetter, S. S. (1943): *Med. Bull. Vet. Admin.*, 20, 58.

Ministry of Agriculture and Fisheries (1945): "Edible and Poisonous Fungi," H.M. Stationery Office.

Ramsbottom, J. (1923): "Handbook of the larger Fungi", British Museum (Natural History), London, 1946.

—— (1945): "Poisonous Fungi", London.

Seymour, F. R. (1932): *Brit. med. J.*, ii, 220. Mushroom poisoning (translation of article by M. M. H. Limousin and G. Petit, *Bull. de l'Académie de Médicine*, May 24, 1932).

Vander Veer, J. B., and Farley, D. L. (1935): *Arch. int. Med.*, 55, 773.

osteoporosis. This of course occurs in other diseases and in senility. At a later stage an affected joint will show diminution of spacing between the two opposing bones due to cartilage destruction, whilst the bones in proximity to the joint show further osteoporosis.

X-ray of a hand will often give a valuable clue. Slight osteoporosis will be noted, or there may be a disturbance of "bone density balance" giving the bones a ground-glass appearance. Careful scrutiny, especially with a magnifying glass, of the heads of the metacarpals and bases of the phalanges may show surface erosions at the articular margins in the neighbourhood of the attachment of the capsule, each erosion showing a fine trabecular outline. There is invariably some attempt at repair as shown by sclerosis at the base. Such erosions, which are obvious when the disease has progressed, may be detected at a very early stage.

ANKYLOSING SPONDYLITIS

It is probable that this disease has been correctly termed "adolescent spondylitis"; it is doubtful if the American view, that it is a form of rheumatoid arthritis, is correct. In few diseases is early recognition more important, for with correct therapy at an early stage of the disease, complete arrest can be obtained in nearly every case. Diagnosis can be made only by radiography.

Symptoms.—The presenting symptom is persistent pain and stiffness in the back, especially low backache. Not infrequently fleeting pains in any part of the body have antedated the back symptoms. The onset is extremely insidious. Controversy exists as to whether the sacro-iliac joints are affected first and the inflammation of the spine follows at a later stage, although this stage may be brief in time or more commonly protracted for several months. It has been stated that on occasions the posterior intervertebral articulations, especially in the lumbo-sacral area, may be attacked whilst there is no radiological evidence of sacro-iliac arthritis. Be that as it may, the basic factor in diagnosis is a skiagram of the sacro-iliac joints. It cannot be emphasized sufficiently often that every young adult with a persistent backache should have the sacro-iliac joints X-rayed, in addition to the vertebræ in proximity to the pain.

Sex ratio.—Men are affected in the ratio of at least 10 to 1 as compared with women.

Age incidence.—It is essentially a disease of adolescence, affecting mostly those in their twenties.

Laboratory findings.—The sedimentation rate is invariably and markedly increased and, as in rheumatoid arthritis, it precedes or lags behind the clinical signs. Anæmia is present.

Radiography.—In viewing the sacro-iliac joints it must be remembered that there are marked normal variations. In practically every case of early ankylosing spondylitis there will be a blurring of the edges of the opposing

metacarpo-phalangeal joints; and wasting of the dorsal interossei muscles. Wasting of the 2nd, 3rd or 4th muscles gives a curious effect, as though a cheese scoop had gouged a groove on the back of the hand between the metacarpals; wasting of the 1st gives the impression that the thumb is stuck on to the rest of the hand and is no longer an independent digit.

Other points to be noted are smooth shiny changes in the skin of the dorsum of the hand, and cold and clammy palms. The wrists may show synovial swelling, whilst there is flattening of both the front and back of the forearms, looking for all the world as though a carpenter's plane had levelled them flat. On the back of the forearm, just below the olecranon, may be found one or more hard painless nodules attached to the deep fascia but over which the skin is freely movable; nodules, however, are usually a *late* sign.

Whilst these changes are taking place in the hands, *the feet* are also affected. Examination will show marked dorsal retraction of the toes with extreme flattening of the metatarsal arch. It is almost the rule that the extremities are affected first, with slow progression to the less peripheral joints, but occasionally there is no immediate centrifugal effect, and the large joints of the body are affected first and possibly for some time before the extremities. The involvement of two or more such joints, without apparent cause, especially if they are symmetrical, will be suggestive of rheumatoid arthritis. The diagnosis is clinched when the hands become affected. As regards the individual joints, it is unusual for the hip joints, sacro-iliac joints or spine to be involved, whereas the knees, ankles, shoulders, elbows, temporo-mandibular or sterno-clavicular joints are commonly affected.

The onset tends to be insidious with vague fleeting pains over several weeks, but occasionally no prodromal symptoms are present and the patient wakes up at a normal hour to find the finger joints stiff, swollen, and painful. Pyrexia in the early stages of the disease may be met with; loss of weight and asthenia are frequent complaints.

CLINICAL FINDINGS

Sex ratio.—Women are affected as compared to men in the ratio of about 10 to 1.

Age incidence.—It may occur between seven and seventy years of age, but predominantly it occurs in women of child-bearing age, with an optimum incidence in the fourth decade of life.

Laboratory findings.—The sedimentation rate is greatly increased: indeed the rate may be the maximal possible. It is worthy of note that the increased rate precedes the clinical signs; conversely, there is a lag behind clinical improvement, in the decrease of the rate. There is almost invariably a marked hypochromic anæmia with a tendency to microcytosis.

Radiography.—The earliest detectable change is a slight generalized

destruction at this point, together with local narrowing of the joint space. Later there is a flattening of the head of the femur with a general narrowing of the joint space, so much so that the latter may appear obliterated; ankylosis never takes place. Accompanying this there is sclerosis of the subarticular bone. Lipping of the articular margins is present and in some cases leads to profuse osteophytic outgrowths.

GOUT

It is impossible to divide gout into two clear-cut entities, tophaceous and non-tophaceous. It is a strange fact that the classical type of tophaceous gout, e.g. nodules in the ears, chalk stones extruding from the knuckles or toes, is rare and has become increasingly so in the last two decades. Recognition of such a condition is easy, but in any case it is a late stage. Non-tophaceous gout, however, is by no means an uncommon disease. Every case of non-tophaceous gout has a tendency to biurate precipitation, although the latter may be only microscopical. It is possible that many cases of gout are labelled fibrositis, neuritis or some other rheumatic complaint, whereas the true nature of the disease is not recognized. On rare occasions gout even simulates rheumatoid arthritis. There is no doubt that the disease is hereditary. It is not acquired but manifests itself in a susceptible individual, given suitable environment. A family history is seldom readily obtainable, but in the majority of cases a history of chronic "rheumatism" or arthritis, may be elicited if the two previous generations are critically reviewed.

Man in the course of his evolution would appear to have lost the liver enzyme uricase which assists in the breakdown of uric acid, an intermediate stage between the complex nitrogenous substances the purins and urea. The frequency with which a high blood uric acid is associated with gout may be due to an alteration of the kidney threshold or, more probably, to an inability of the individual to conjugate uric acid with some other substance, such a conjugation facilitating the excretion of uric acid and preventing deposits in the tissues.

Many kinds of rich food and good drink have been accused of producing gout. Doubt, however, has recently been cast on this view by American investigators, who were unable to produce a flare-up in gouty patients when such supposedly precipitating articles were administered over a long period of time. Moreover, non-tophaceous gout is quite common in these present days of austerity. Yet a gastro-hepatic upset frequently produces an attack. Some patients indeed are allergic to a particular article of diet. Trauma, whether major or minor, is a fairly common cause of an acute attack.

Signs and symptoms.—It is only on occasions that the classical manifestation of acute gout is present in the big toe joint, which is then hot, swollen, dusky red with a central bluish tinge and exquisitely tender. Such an attack occurring in an otherwise healthy adult is pathognomonic of gout. Often, however, other joints or parts of the body may be affected for years before

bony surfaces. There may be a generalized slight osteoporosis of the spine. There may also be early blurring of the outline of the facets of the posterior articular processes, either general or localized to certain areas. Much later, fusion occurs, and there is a generalized ossification of the intervertebral ligaments.

OSTEOARTHRITIS

As in the previous disease, there is only one way to recognize this condition early and that is by X-ray examination. The onset is insidious and clinical signs and symptoms vary; they may simulate other diseases or may be entirely absent, but the radiological appearance is characteristic.

Suggestive *symptoms* are aching in a joint or joints when fatigued, relief of symptoms after a night's rest, to be followed possibly some time later by further aching after similar strain of work or walking. Eventually the remissions become less frequent and pain becomes constant.

Osteoarthritis may be present in only one joint or more commonly be present in several joints in varying degrees. A hip joint may be taken to illustrate the disease. Pain is usually situated in the upper and medial aspect of the thigh. At times the pain may be referred to the back and be mistaken for lumbago. Not infrequently the pain is referred to the knee, and an arthritis of the knee or a sciatica' is suspected. The earliest sign of hip involvement is limitation of external rotation at the hip joint. At the same time (and invariably later), there may be limitation of abduction or adduction.

There is considerable controversy as to the cause of the pain, since severe degrees of osteoarthritis may be present without pain. It is suggested that it may be due to pressure or trauma of the extra-articular hypertrophic villous structures which develop around the borders of the osteoarthritic joint. Or again it may be due to an accompanying capsulitis, adhesions at the insertion of the ligaments, and spasm in the corresponding muscles.

A regime directed to relieving these defects by regular daily active non-weight-bearing exercises to the hip, with a degree of limitation to the patient's weight-bearing activity, is of the utmost benefit if the condition be recognized sufficiently early. At a later stage, when irreversible changes have taken place, such as subluxation, however slight, of the head of the femur, nothing save a walking appliance or surgery offers any hope of permanent benefit.

Sex ratio.—It is more frequent in men than in women.

Age incidence.—As a rule the onset is in the late forties or early fifties.

Laboratory findings.—These, including the sedimentation rate, are invariably normal.

Radiography.—Early changes are articular overlapping of the extremity of the neck of the femur and the appearance of small cystic areas in the juxta-articular bone, particularly in the superior lip of the acetabulum and the opposed surface of the femoral head. This is followed by local articular

destruction at this point, together with local narrowing of the joint space. Later there is a flattening of the head of the femur with a general narrowing of the joint space, so much so that the latter may appear obliterated; ankylosis never takes place. Accompanying this there is sclerosis of the subarticular bone. Lipping of the articular margins is present and in some cases leads to profuse osteophytic outgrowths.

GOUT

It is impossible to divide gout into two clear-cut entities, tophaceous and non-tophaceous. It is a strange fact that the classical type of tophaceous gout, e.g. nodules in the ears, chalk stones extruding from the knuckles or toes, is rare and has become increasingly so in the last two decades. Recognition of such a condition is easy, but in any case it is a late stage. Non-tophaceous gout, however, is by no means an uncommon disease. Every case of non-tophaceous gout has a tendency to biurate precipitation, although the latter may be only microscopical. It is possible that many cases of gout are labelled fibrositis, neuritis or some other rheumatic complaint, whereas the true nature of the disease is not recognized. On rare occasions gout even simulates rheumatoid arthritis. There is no doubt that the disease is hereditary. It is not acquired but manifests itself in a susceptible individual, given suitable environment. A family history is seldom readily obtainable, but in the majority of cases a history of chronic "rheumatism" or arthritis, may be elicited if the two previous generations are critically reviewed.

Man in the course of his evolution would appear to have lost the liver enzyme uricase which assists in the breakdown of uric acid, an intermediate stage between the complex nitrogenous substances the purins and urea. The frequency with which a high blood uric acid is associated with gout may be due to an alteration of the kidney threshold or, more probably, to an inability of the individual to conjugate uric acid with some other substance, such a conjugation facilitating the excretion of uric acid and preventing deposits in the tissues.

Many kinds of rich food and good drink have been accused of producing gout. Doubt, however, has recently been cast on this view by American investigators, who were unable to produce a flare-up in gouty patients when such supposedly precipitating articles were administered over a long period of time. Moreover, non-tophaceous gout is quite common in these present days of austerity. Yet a gastro-hepatic upset frequently produces an attack. Some patients indeed are allergic to a particular article of diet. Trauma, whether major or minor, is a fairly common cause of an acute attack.

Signs and symptoms.—It is only on occasions that the classical manifestation of acute gout is present in the big toe joint, which is then hot, swollen, dusky red with a central bluish tinge and exquisitely tender. Such an attack occurring in an otherwise healthy adult is pathognomonic of gout. Often, however, other joints or parts of the body may be affected for years before

the toe joint is involved. The first attack on the joints is commonly non-articular. There may be accompanying malaise and pyrexia. The shoulder, temporo-mandibular and sterno-clavicular joints are rarely affected: this is in contrast to rheumatoid arthritis. Moreover, the acute attack occurs in the early hours of the morning and wakens the patient. The symptoms are readily relieved by adequate dosage of colchicine: this in itself is of diagnostic importance. Prodromal symptoms are absent. Complete remissions occur.

Swelling of an olecranon bursa and to a lesser degree bursitis under the tendo Achilles are often early signs. If such a bursa is incised a whitish pultaceous discharge may result for many months, similar to the discharge from a tophaceous mass. "Fleshy" nodules may be present in the sub-cutaneous tissue on the dorsum of one or more fingers, especially in the neighbourhood of the mid-phalangeal joints; whilst on the palmar aspect there may be seen glistening white areas of the digital sheath. Suggestive signs are sausage-like enlargement of the whole of several fingers, usually of both hands, but occasionally confined to one hand: also swelling accompanied by pain at the base of a thumb. Examination of the latter will show a synovitis of the metacarpo-trapezius or the metacarpo-phalangeal joint, with prominent veins coursing over the swelling.

Sex ratio.—It is said that about 95 per cent. of sufferers are men. This may be true of the tophaceous type, but it is quite untrue of the non-tophaceous: more women suffer from non-tophaceous gout than men.

Age incidence.—Although it may occur occasionally in the young or the old it is essentially a disease that manifests itself between the fourth and sixth decades.

Laboratory findings.—The blood uric acid is usually raised at some period, but many cases of gout have normal values and therefore it must be realized that this test is not a reliable indicator. In the active phase the sedimentation rate may be increased moderately, occupying an intermediate position between the normal rate in osteoarthritis and the greatly increased rates in rheumatoid arthritis and spondylitis. There is no anæmia.

Radiography.—Osteoporosis is absent. There may be evidence of soft-tissue swelling during the acute phase and this may become permanent at a later stage, should there be a deposition of subcutaneous tophi. Destruction of articular cartilage, as evidenced by loss of joint spacing, takes place after the disease has been present for some time. In special localities, the fingers, wrists, distal ends of radius and ulnar, and the feet, areas of destruction appear in the cancellous bone, often at an early stage. These *erosions* are sharply defined, punched out as it were, cystic, semi-opaque, and structure-less. There is no evidence of sclerosis in the neighbourhood. All this should be contrasted with the erosions in rheumatoid arthritis. As in the latter disease, a "diagnostic" skiagram of the hand, even though clinical signs are locally absent, may help in early recognition.

REVISION CORNER

This section is devoted to short articles in which experts summarize modern treatment and clinical procedures, particularly for the benefit of general practitioners who have returned from the Forces.

LEUCORRHŒA

LEUCORRHŒA is a very common gynæcological complaint. The name implies that the discharge is white in colour; this therefore excludes markedly purulent discharges such as those due to *Trichomonas vaginalis* or *Monilia albicans*. The discharge may be sufficient in quantity to be noticed by the patient and for it to cause distress by its presence, or to give rise to chafing and secondary skin lesions. The origin of the discharge is either from an excess of the normal secretions of the vagina and cervix, or is due to mucoid discharge from the cervix subsequent to chronic infections which have changed the amount of glandular tissue in the cervix (e.g. erosions, chronic gonorrhœa).

ETIOLOGY

The normal vaginal fluid derives by transudation from the cells of the vaginal epithelium and is mixed with the secretions from the upper genital passages. Microscopically the contents consist of desquamated squames from the vaginal wall, numbers of leucocytes and, during adult life, quantities of the *Bacillus vaginalis* (Doderlein's bacillus). The reaction of the fluid is acid (pH 4—5), the acidity being due to lactic acid produced from the glycogen of the vaginal epithelium. The presence of glycogen is associated with the action of œstrin on the epithelium and hence is characteristic of adult life when the ovaries are functioning normally. The amount of secretion may vary considerably with the general health of the patient, pregnancy, or excessive secretion by the cervical glands, e.g. nulliparous erosion, and theoretically excessive œstrin action may be an associated cause. Such increase in the discharge may be considered as of physiological origin. Normally in adult life the high acidity of the fluid makes it antiseptic to most pathogenic organisms, hence vaginitis, except that due to *Trichomonas vaginalis* or *Monilia*, is uncommon. Before puberty, however, and after the menopause, when the fluid has almost a neutral reaction, infections are more likely to occur and will give rise to a purulent discharge.

During adult life leucorrhœa may also arise pathologically from increase in the cervical secretions subsequent to infection or due to congestion by retroversion or fibroids. The discharge in these cases is colourless, white or mucoid, and is due to erosion, ectropion, and laceration of the cervix subsequent to child-birth or gonorrhœa.

INVESTIGATIONS REQUIRED

Investigation of a case of leucorrhœa demands therefore consideration of the history (age, parity, past infection), local examination to note the type of discharge and to make sure that it is not a purulent one and to ascertain the state of the vagina and cervix, and pathological examination to determine whether pus is present, the pH, and the presence of normal (Doderlein) or abnormal vaginal flora. This full pathological investigation will in many cases determine the treatment; e.g., if the patient is a child and the discharge is found to contain Doderlein's bacilli in profusion it is practically certain to be associated with anæmia or poor general health and to need no local treatment, whereas if the discharge contains pus then examination under an anæsthetic would be the next step.

TREATMENT

In cases of *simple physiological leucorrhœa* treatment depends upon general measures, such as the administration of iron for anæmia, the avoidance of constipation, and a generally healthy life. A simple saline or sodium bicarbonate douche [60 grains (3.9 gm.) to one pint (0.6 litre) of water] may be necessary if the discharge gives rise

to skin lesions or should stain the clothes. During *pregnancy* the discharge should not be treated unnecessarily by douches or pessaries but the patient should be instructed to sponge down with the bicarbonate solution and to dry the parts thoroughly. In view of what has been said above of the possibility of endocrine stimulus causing discharge it might be inferred that treatment to counteract it would be indicated. In practice, however, it is valueless.

In cases in which *local cervical lesions* are found, treatment of these is indicated. The days of local caustic therapy have passed. If simple astringent douches (zinc or alum) do not give relief then cauterization of the cervix in a linear radiate manner is the best treatment. This can be done with either an electric or Pacquelin cautery, but some prefer to use diathermy. If the cervix is badly lacerated, amputation will usually have to be performed.

<div align="right">KENNETH BOWES, M.D., M.S., F.R.C.S.</div>

TOXÆMIA OF PREGNANCY

UNDER this title consideration will be given to the conditions known as "the pregnancy kidney", toxic albuminuria, albuminuria of pregnancy or pre-eclampsia, with their possible termination in eclampsia. There are certain other diseases known as "toxæmias of pregnancy", for instance hyperemesis gravidarum, and it is probably better to give up the term "toxæmia" and adopt pre-eclampsia to cover all cases of albuminuria which are not due to pre-existing renal damage. The cardinal signs of this disease are a rising blood pressure, albuminuria and œdema. Any of these signs may be present alone and may progress occasionally to eclampsia without association with the other two. For that reason alone the disease should not be known as "albuminuria of pregnancy", as by waiting for the occurrence of albuminuria, before adopting treatment, fits may occur.

In a brief article of this nature there is no place for a detailed inquiry into the etiology of the disease. Suffice it to say that in spite of all the recent interesting work on hormones there is no conclusive evidence as yet to incriminate them as being the fundamental cause—although eventually some endocrine imbalance may well prove to be the answer which at the moment is still shrouded in mystery. On the other hand, there is reasonably conclusive evidence to show that patients given extra supplies of calcium and mixed vitamins are less likely to develop pre-eclampsia than those on poorer diets.

Therefore the essential duty is to ensure that antenatal patients are receiving an adequate diet and ever to be on the lookout for early signs of pre-eclampsia. The condition may then be treated in its early stages and the severe sequelæ of the birth of premature infants and macerated still-births, eclampsia, and slowly progressive arteriosclerotic kidneys in the mother may be prevented.

ANTENATAL CARE

Patients should be seen early in pregnancy in order to determine their "basal" blood pressure and to exclude the presence of any previous renal or hypertensive disease, both of which may proceed to pre-eclampsia and eclampsia. Advice should be given at this early visit on dietetic factors and stress should be laid on the importance of carrying out the advice given and taking the various tablets prescribed. With knowledge of these "basal" factors, further monthly examinations should be made and the blood pressure checked and the urine examined on each occasion; whilst a careful check on the increase in the patient's weight may, if it is above five pounds a month, be an early sign of impending pre-eclampsia. During the last ten weeks similar investigations should be carried out at fortnightly intervals until the thirty-sixth week and subsequently at weekly intervals until delivery.

TREATMENT

Mild cases.—Should the blood pressure be found to be rising slightly, the diastolic figure being the more important, and slight pitting œdema of the shins be present

with a trace of albumin in a clear specimen of urine, then the maximum amount of rest must be insisted upon and any tendency to constipation should be corrected with small doses of salines. Reduction of the meat intake is unnecessary under the present rationing system and may even be harmful, but the diet may be increased by extra carbohydrates in the form of glucose. Should œdema be marked, added salt, either in cooking or at table, should be forbidden. This regime will be all that is necessary for the milder cases but these patients should subsequently be seen at weekly intervals at least.

Moderate cases.—Should the blood pressure reach 150/100 mm. Hg, or albuminuria occur with a slightly lesser blood pressure, and œdema be present, complete rest in bed must be the rule. The diet should be ordered as for the mild cases described above. The blood pressure should be recorded daily and the amount of albuminuria estimated daily in an Esbach's tube. The fœtal heart should also be auscultated daily. Should œdema be marked, a fluid intake and output chart should be kept and the amount of fluids taken during the day should be reduced to not less than one pint, particularly if the output falls below 30 ounces (840 c.cm.) in the day. Under these conditions, even with improvement, and earlier if there is deterioration, pregnancy should rarely be allowed to continue for more than two weeks; the exception perhaps being in cases of this severity occurring at about the thirty-second or thirty-third week, when an extra week or two may make all the difference in the chances of the survival of the premature baby.

Severe cases.—Occasionally patients are first seen with the premonitory symptoms of eclampsia—mistiness of vision, flashes of light before the eyes, severe fronto-occipital headaches, vomiting and epigastric pain. The blood pressure is usually high, in the neighbourhood of 180/110 mm. Hg, and the albuminuria may reach 0.6 per cent. or more. Under these conditions strong sedatives are necessary; morphine $\frac{1}{4}$ grain (0.016 gm.) is probably the best. Fluids only should be allowed by mouth and full doses of magnesium sulphate are useful. If there is no improvement within twenty-four to forty-eight hours, labour should be induced as soon as possible, whilst rarely Cæsarean section is the safest and most expedient method of delivery, particularly if the signs become more severe or the chances of labour starting very soon after induction are poor.

Eclampsia.—When fits have occurred, their further prevention and delivery as soon as possible by the safest method are the essential aims of treatment. The fits are due to the marked sensitivity of the central nervous system, possibly on account of œdema of the brain or cortical vascular spasm. Adequate sedation is therefore of prime importance. Morphine is the best drug to use and it may be repeated if necessary up to 1$\frac{1}{2}$ grains (0.1 gm.) in twenty-four hours. It should be combined either with chloral, 30 grains (2 gm.) by mouth or 40 to 60 grains (2.65 gm. to 4 gm.) per rectum if vomiting is severe, or combined with paraldehyde, 360 minims (21 c.cm.) per rectum. It is doubtful whether gastric or colonic lavage achieves any object. Magnesium sulphate, 4 ounces (114 c.cm.) of saturated solution per rectum, may help to reduce cerebral œdema. The patient should be nursed in a darkened room and her position in bed must be changed from time to time to reduce hypostatic pulmonary congestion—and the tongue must be prevented from falling back into the throat and blocking the airway. Fits should be controlled by light chloroform narcosis, the minimum amount should be given to minimize any further liver damage it may produce. If fits are very frequent a small venesection is useful, and if cyanosis and pulmonary œdema are marked oxygen and atropine are valuable. Calcium gluconate, 10 c.cm. of 10 per cent. solution, may be given intravenously and repeated small infusions of 20 per cent. glucose saline may greatly reduce cerebral œdema.

Labour, if not in progress, usually begins after fits have occurred and is often extremely rapid. No obstetrical interference other than an instrumental delivery

to skin lesions or should stain the clothes. During *pregnancy* the discharge should not be treated unnecessarily by douches or *pessaries* but the patient should be instructed to sponge down with the bicarbonate solution and *to dry the parts* thoroughly. In view of what has been said above of *the possibility of endocrine stimulus causing discharge* it might be inferred that treatment to *counteract it* would be indicated. In practice, however, *it is valueless.*

In cases in which *local cervical lesions* are found, treatment of these is indicated. The days of local caustic therapy have passed. If simple astringent douches (zinc or alum) do not give relief then cauterization of the cervix in a linear radiate manner *is the* best treatment. This can be done with either an electric or Pacquelin cautery, but some prefer to use diathermy. If the cervix is badly lacerated, amputation will usually have to be performed.

Kenneth Bowes, M.D., M.S., F.R.C.S.

TOXÆMIA OF PREGNANCY

Under this title consideration will be given to the conditions known as "the pregnancy kidney", *toxic albuminuria,* albuminuria of pregnancy or pre-eclampsia, with their possible termination in eclampsia. There are certain other *diseases known* as "toxæmias of pregnancy", for instance hyperemesis gravidarum, and it is probably *better to give up the term* "toxæmia" and adopt pre-eclampsia to cover all cases of albuminuria which are not due to pre-existing renal damage. The cardinal signs of this disease are a rising blood pressure, albuminuria and œdema. Any of *these signs* may be present alone and may progress occasionally to eclampsia without association with the other two. For that reason alone the disease should not be known as "albuminuria of pregnancy", as by waiting for the occurrence of albuminuria, before adopting treatment, fits may occur.

In a brief article of this nature there is no place for a detailed inquiry into the etiology of the disease. Suffice it to say that in spite of all the recent interesting work on hormones there is no conclusive evidence as yet to incriminate them as being the fundamental cause—although eventually some endocrine imbalance may well prove to be the answer which at the moment is still shrouded in mystery. On the other hand, there is reasonably conclusive evidence to show that patients given extra supplies of calcium and mixed vitamins are less likely to develop pre-eclampsia than those on poorer diets.

Therefore the essential duty is to ensure that antenatal patients are receiving an adequate diet and ever to be on the lookout for early signs of pre-eclampsia. The condition may then be treated in its early stages and the severe sequelæ of the birth of premature infants and macerated still-births, eclampsia, and slowly progressive arteriosclerotic kidneys in the mother may be prevented.

ANTENATAL CARE

Patients should be seen early in pregnancy in order to determine their "basal" blood pressure and to exclude the presence of any previous renal or hypertensive disease, both of which may proceed to pre-eclampsia and eclampsia. Advice should be given at this early visit on dietetic factors and stress should be laid on the importance of carrying out the advice given and taking the various tablets prescribed. With knowledge of these "basal" factors, further monthly examinations should be made and the blood pressure checked and the urine examined *on each occasion;* whilst a careful check on the increase in the patient's weight may, *if it is above five* pounds a month, be an early sign of impending pre-eclampsia. During the last ten weeks similar investigations should be carried out at fortnightly *intervals until* the thirty-sixth week and subsequently at weekly intervals until delivery.

TREATMENT

Mild cases.—Should the blood pressure be found to be rising slightly, the diastolic figure being the more important, and slight pitting œdema of the shins be *present*

perception, are presented in the same way until stereoscopic vision is obtained. It is then necessary to attempt the reduction of the angle of squint by increasing the amplitude of fusion. This implies maintaining fusion during angular movements of the pictures towards the normal position. In some cases, especially those associated with refractive errors, cure is possible by means of orthoptics alone, since once stereopsis is attained the eyes may be held straight in order to avoid the diplopia which would result from any deviation. In some cases, however, operation is required as well and in all cases except those which are practically emmetropic the error of refraction must be corrected by spectacles. The usual sequence of events in treating a child with a squint is the prescription of glasses as soon as the squint is noticed (even as young as six months), the stimulation of binocular vision when it is old enough, an operation to reduce the angle of squint and a final course of orthoptics to consolidate fusion with the eyes in the improved position. Such a treatment may take seven to eight years, but will in a high proportion of cases result in the possession of two useful eyes, a fair grade of depth perception and an excellent cosmetic result which will be permanent. On the other hand, the older treatment of correcting the error of refraction and operating for cosmetic reasons is apt to leave the patient with one amblyopic eye and with the risk of convergence or divergence developing some years later and necessitating further operation.

In cases of *paralytic squint*, orthoptics also has a place. Combined with operation it often produces an unexpectedly good result, especially in traumatic cases. This line of treatment for paralytic squint and its consequent diplopia has been much developed during the war and has given hope of ameliorating a type of disability previously considered inoperable and certain to end in monocularity or diplopia.

It is, however, in the treatment of the *phorias* or *latent squints* that orthoptics produces from the patient's point of view the most satisfying results. These patients often suffer great disability from constant eye strain, ocular headaches and inability to do close work. Their visual acuity is often perfect and their error of refraction slight. They almost always wear glasses, since an attempt will have been made to alleviate the symptoms by correcting any abnormality present. Their real trouble is, however, due to their imperfectly adjusted binocular mechanism, and if their amplitude of fusion, accuracy of depth perception and voluntary control over convergence and other eye movements, can be improved most of their symptoms will disappear, and a number, especially of the young low-grade hypermetropes, will be able to discard their glasses entirely. It is largely due to these successes that the popular opinion prevails that eye exercises can cure errors of refraction. This they never do, but they undoubtedly do help the patient to make better use of the kind of eyes he has. The increase in voluntary control and in the understanding of the act of seeing which results from these exercises also increases the patient's confidence in his ability to use his eyes. Many of these patients exhibit neurotic symptoms and show great fear over their sight. Whether the neurosis is engendered by the discomfort of the phoria, or *vice versa*, is not certainly known, but it is indubitable that the vicious circle can in a large number of cases be broken by orthoptic treatment.

As stated above, treatment for true squint should be started as early in life as possible. Treatment for paralytic squint can of course be considered at any age. Treatment for the asthenopic symptoms of patients with phorias is usually indicated in young adults, since they are the most frequent sufferers. It can, however, be given up to any age, even patients of sixty-five having been known to benefit, although the best results are obtained in persons not yet presbyopic.

It is thus obvious that orthoptic treatment, properly supervised and often combined with operation and prescription of glasses, should always be considered in any case of imperfect binocular vision.

PROFESSOR IDA MANN, D.Sc., M.B., B.S., F.R.C.S.

early in the second stage or rupturing the membranes when the cervix is about ½ dilated is justifiable. Cæsarean section is only indicated if some other major complication is present or the eclampsia has been of the rare fulminating type in which a fit has occurred within a very short time of the first signs of pre-eclampsia (used in its broad sense as indicated at the beginning of this article). Should labour not begin after the fits have been controlled the membranes should be ruptured within the next three or four days.

Sedatives should be continued for the first two or three days of the puerperium, care being taken to avoid too great a respiratory depression with its risks of pulmonary complications.

BRAITHWAITE RICKFORD, M.D., F.R.C.S., M.R.C.O.G.

ORTHOPTICS

ORTHOPTICS is the name given to a form of treatment designed to produce or to improve binocular stereoscopic vision. In conception it is of a certain antiquity, exercises and apparatus for the treatment of squint being in use in the seventeenth century. In its present highly developed form, however, it dates roughly from the beginning of this century and can be considered as by no means static at the present time. The actual treatment is usually given by medical auxiliaries (orthoptists) who work under the direction of ophthalmic surgeons, not many of whom have themselves the time to train their patients. The nature and potentialities of orthoptic exercises must be thoroughly understood by the practitioner in order to avoid disappointment following undue optimism as to their capabilities. Since the public at the moment is strongly in favour of "eye exercises" the treatment is popular and may even be requested by the patient, who has seldom, however, any clear conception of what "eye exercises" can actually accomplish.

Two main groups of cases are apparent: In the first group, the true squints, the object under direct observation is not looked at by both eyes at the same time. One eye looks at it (i.e., receives its image on the macula), the other is turned at such an angle that the image does not fall on the macula. This image is ignored and therefore the patient does not complain of diplopia, although if the squint is of recent or sudden onset this may be noticed. In the second group, the phorias, the object is seen by both maculæ at the same time, but only with a certain muscular effort, since the position of optimum comfort for these patients is not one of parallelism of the optic axes. In other words, they have a latent squint which they overcome in order to achieve binocularity and depth perception (stereopsis). The true squints also fall into two main groups, i.e., concomitant and paralytic. In the former all the normal movements can be performed by each eye separately, but when both eyes are in use the coordination between them breaks down and the images do not fall on corresponding points on the two retinæ. In the paralytic group there is a failure (from a peripheral cause) of certain movements only.

The use of orthoptic treatment for *concomitant squint* is advisable provided the patient is fairly young, i.e., roughly under twelve years of age, and preferably between four and five. The treatment is divided into stages, the first being the restoration of a certain visual acuity to the squinting eye by occlusion of the eye which fixes, combined with exercises in the simultaneous perception of two dissimilar pictures thrown one on each macula. When simultaneous perception has been achieved the next stage is attempted, namely, the building up of the fusion sense. This is done by presenting two slightly incomplete pictures to each of the two eyes, the combined result being a complete picture. When the patient sees the picture correctly combined from its components he has attained simple fusion. The eyes are still in the squinting position, the correct position of the images on the macula being assured by the apparatus through which the pictures are viewed.

When *simple fusion* is present more complicated pictures, involving depth

Simple cold spring waters are bottled at Evian and are similar to the table waters from Malvern. Radio-active thermal waters are usually of low mineralization and contain some calcium salts, their proven action being the production of diuresis. There is some evidence that they are uric acid solvents. They are obtained at such spas as Bath, Buxton Aix-les-Bains and Baden-Baden. The radio-activity, whatever its effect may be, rapidly disappears on keeping. Mineralized waters, containing chlorides, sulphates and sulphides are mainly aperient and hepatic stimulants. They vary greatly, both with regard to the concentration and relative proportions of their constituent salts. The springs at Cheltenham and Leamington contain mainly chlorides and sulphates; Harrogate and Llandrindod Wells, sulphates and sulphides. The waters of Contrexéville and Vittel, however, contain the sulphate of calcium instead of that of magnesium or sodium and are therefore diuretic, resembling more closely in these properties the waters found in this country at Bridge of Allan and to a lesser degree those of Bath and Buxton. The carbonated salines are the fourth group and are not well represented in this country. Vichy water is of the alkaline subgroup of this type. These various waters may have a beneficial effect, both from the psychological point of view and by encouraging a greater intake of fluids, those of low mineralization and containing calcium salts being of special use in gout on account of their diuretic action. The laxative effect of others may again be usefully employed in the eliminative treatment of many fibrositics and over-weight osteoarthritics. The British spas have never attempted to contend with the foreign spas in the market in bottled waters and the only ones at present available, except at their source, are those of Bath, Buxton, Cheltenham, Harrogate, Leamington and Malvern.

G. D. KERSLEY, M.D., F.R.C.P.

The Choice of Obstetric Forceps

QUERY.—I have read in the "Revision Corner" of the January 1946 issue of *The Practitioner*, the helpful indications for obstetric forceps by Dr. Charles Read, and his up-to-date personal consideration on the subject. It would have been still more helpful, however, if he had added his views concerning the relative merits of the types of forceps in general use. Jellett and Madill, in their textbook on midwifery, p. 1095, say that those who are accustomed to any particular pattern of forceps consider that pattern the best and, unless they find one which offers a manifest improvement, are unwilling to change. At the time of writing (1929) they

seemed to prefer Neville's axis-traction forceps. I shall be glad to hear Dr. Read's personal views, and also as regards Kielland's forceps.

REPLY.—Generally speaking there is the choice of either Neville's axis-traction forceps or Milne Murray's axis-traction forceps. For the expert, the Milne Murray provides the truest traction but is a more complicated instrument, and for all practical purposes the Neville's instrument is probably the most useful. I would therefore advise your correspondent to obtain the latter. In respect of Kielland's forceps, this instrument was invented entirely for delay in the late first stage and second stage at the pelvic brim due to a flat pelvis with a transverse arrest of the head, and thus the blades of the forceps must be applied in relation to the head and not in relation to the pelvis. The Kielland's forceps have no pelvic curve, and consequently they have been used as rotators in cases of occipito-posterior position and deep transverse arrest. In expert hands the results obtained are excellent, but for the occasional obstetric operator they present difficulties and their use is not without danger.

CHARLES D. READ, M.B., F.R.C.S.ED.,
F.R.A.C.S., F.R.C.O.G.

The Control of Chronic Alcoholism

QUERY.—Can you give advice on what can be done with the following patient?—A man aged thirty-six; a chronic alcoholic. He started drinking at the age of eighteen. There is a tendency for drink in the family. He has been in numerous homes for cure, but always discharged himself after a few days. He has seen several doctors and has had various treatments, without any lasting result. There are sober intervals for two or three weeks and then he becomes quite normal mentally and much improved physically. Does the law provide any means of control for this type of patient?

REPLY.—Unfortunately English law makes practically no provision for the drunkard who is a curse to himself and his family. If he is certifiably insane when comparatively sober he may be dealt with under the Lunacy Act, 1890; and if he behaves when drunk in some way which will bring him within the criminal law, e.g., by committing a serious assault or attempting suicide, he may be committed to an institution for inebriates. This, however, is hardly ever done and is of little use, because the drunkard is not likely to cooperate in his treatment. So far as the law is concerned the problem is insoluble.

D. HARCOURT KITCHIN
Barrister-at-Law.

NOTES AND QUERIES

Alkalis in Impaired Renal Function

QUERY.—In his article on "Renal Disease and Its Treatment" (May 1946, **156**, 368), Prof. Robert Platt makes no reference to the use of alkalis in the treatment of (a) acute nephritis or (b) sulphonamide anuria. What is the present position with regard to the use of alkalis in impaired renal function?

REPLY.—(1) There was a vogue at one time for giving alkalis in acute nephritis. There has never been any proof that they do good, and no doubt they were largely used to satisfy a desire to prescribe something for a disease in which medicinal treatment has usually no place. The proper treatment by rest, warmth and fluid restriction makes the use of medicines quite unnecessary, and they are liable to distract the attention of the doctor and nurses from the more important measures.

(2) The intensive alkali treatment of nephrosis described by Osman many years ago apparently achieved results in a few cases, but it is not free from danger and has been given up by most physicians. No less an authority than Fishberg simply states that he has no experience of it.

(3) In certain cases of terminal chronic nephritis, including the type associated with renal dwarfism, a true acidosis occurs and is accompanied by renal dyspnœa. This is undoubtedly amenable to treatment by alkali, but the nature of the underlying disease renders such treatment merely palliative.

(4) I mentioned that sulphonamide anuria was less likely to occur if alkali was prescribed regularly whenever sulphonamides were administered. I omitted to state that it is wise to give alkali as well as copious fluid should sulphonamide anuria occur. This is rational, since the solubility of these compounds, especially the acetyl derivatives of sulphathiazole and sulphadiazine, is greatly increased in an alkaline urine.

PROFESSOR ROBERT PLATT, M.D., F.R.C.P.

Prophylaxis against Typhoid, Paratyphoid, Typhus and Yellow Fever

QUERY.—Following the article in the April issue on "Preventive Inoculation against Infectious Diseases in Childhood", can you furnish me with any details on the preventive inoculation against the typhoid group, typhus and yellow fever, in children? I have a small patient who is going to the tropics and is requiring such inoculation. I would be grateful for the doses in these three instances, with any information on reaction and duration.

REPLY.—(1) *Typhoid and paratyphoid.*—It is recommended that the vaccine used should be that prepared by Felix and his co-workers, containing 22.5 per cent. of alcohol. The reason for recommending this vaccine is that it gives less reaction than the previous vaccines which were used for the prevention of typhoid fever. The doses of the vaccine are given with an interval of three weeks between the injections. The reactions likely to be encountered are very mild and are merely an occasional redness around the site of injection with transient pain in the arm. A general reaction in the form of pyrexia and malaise is not frequently encountered with this vaccine. The dosage is in accordance with the following table:—

Age	Sex	1st Dose	2nd Dose
Adult	Male	0.5 c.cm.	0.5 c.cm.
Adult	Female	0.2 c.cm.	0.4 c.cm.
Children:—			
Under 8 years	M. or F.	0.05 c.cm.	0.05 c.cm.
9-12 years ..	M. or F.	0.05 c.cm.	0.1 c.cm.
13-15 years	M. or F.	0.1 c.cm.	0.2 c.cm.
16-18 years	M. or F.	0.2 c.cm.	0.4 c.cm.

(2) *Typhus.*—Three doses of this vaccine are given at weekly intervals. The dose for an adult is 1 c.cm. and for children under the age of twelve years 0.5 c.cm. Reactions are uncommon, but again if met with consist of pain around the site of the injection with a transient malaise, which will subside within twenty-four hours.

(3) *Yellow fever.*—The dose of this vaccine is 0.5 c.cm. for adults and 0.25 c.cm. for children under twelve years of age. A single dose is given and the reactions encountered are negligible.

W. POWELL PHILLIPS, M.R.C.S., L.R.C.P., D.P.H.

Mineral Waters

QUERY.—What are the indications for the administration of mineral waters in cases of chronic rheumatism? When they are indicated, which are the ones that should be used? I used to prescribe some of the Continental waters, e.g. Vichy and Contrexéville.

REPLY.—The use of most bottled natural waters is surrounded by folk lore, and their use by medical men is prejudiced by the extravagance of commercial advertisements. Yet, to disregard the public opinion of centuries and rule out any therapeutic value because their *modus operandi* is not understood would be unjustifiable. It is permissible, however, to state dogmatically that no specific therapeutic action in rheumatic disease has ever been proven. Any simple classification of waters is arbitrary, as there will necessarily be both overlap and subdivision.

Simple cold spring waters are bottled at Evian and are similar to the table waters from Malvern. Radio-active thermal waters are usually of low mineralization and contain some calcium salts, their proven action being the production of diuresis. There is some evidence that they are uric acid solvents. They are obtained at such spas as Bath, Buxton Aix-les-Bains and Baden-Baden. The radio-activity, whatever its effect may be, rapidly disappears on keeping. Mineralized waters, containing chlorides, sulphates and sulphides are mainly aperient and hepatic stimulants. They vary greatly, both with regard to the concentration and relative proportions of their constituent salts. The springs at Cheltenham and Leamington contain mainly chlorides and sulphates; Harrogate and Llandrindod Wells, sulphates and sulphides. The waters of Contrexéville and Vittel, however, contain the sulphate of calcium instead of that of magnesium or sodium and are therefore diuretic, resembling more closely in these properties the waters found in this country at Bridge of Allan and to a lesser degree those of Bath and Buxton. The carbonated salines are the fourth group and are not well represented in this country. Vichy water is of the alkaline subgroup of this type. These various waters may have a beneficial effect, both from the psychological point of view and by encouraging a greater intake of fluids, those of low mineralization and containing calcium salts being of special use in gout on account of their diuretic action. The laxative effect of others may again be usefully employed in the eliminative treatment of many fibrositics and over-weight osteoarthritics. The British spas have never attempted to contend with the foreign spas in the market in bottled waters and the only ones at present available, except at their source, are those of Bath, Buxton, Cheltenham, Harrogate, Leamington and Malvern.

G. D. KERSLEY, M.D., F.R.C.P.

The Choice of Obstetric Forceps

QUERY.—I have read in the "Revision Corner" of the January 1946 issue of *The Practitioner*, the helpful indications for obstetric forceps by Dr. Charles Read, and his up-to-date personal consideration on the subject. It would have been still more helpful, however, if he had added his views concerning the relative merits of the types of forceps in general use. Jellett and Madill, in their textbook on midwifery, p. 1095, say that those who are accustomed to any particular pattern of forceps consider that pattern the best and, unless they find one which offers a manifest improvement, are unwilling to change. At the time of writing (1929) they

seemed to prefer Neville's axis-traction forceps. I shall be glad to hear Dr. Read's personal views, and also as regards Kielland's forceps.

REPLY.—Generally speaking there is the choice of either Neville's axis-traction forceps or Milne Murray's axis-traction forceps. For the expert, the Milne Murray provides the truest traction but is a more complicated instrument, and for all practical purposes the Neville's instrument is probably the most useful. I would therefore advise your correspondent to obtain the latter. In respect of Kielland's forceps, this instrument was invented entirely for delay in the late first stage and second stage at the pelvic brim due to a flat pelvis with a transverse arrest of the head, and thus the blades of the forceps must be applied in relation to the head and not in relation to the pelvis. The Kielland's forceps have no pelvic curve, and consequently they have been used as rotators in cases of occipito-posterior position and deep transverse arrest. In expert hands the results obtained are excellent, but for the occasional obstetric operator they present difficulties and their use is not without danger.

CHARLES D. READ, M.B., F.R.C.S.ED.,
F.R.A.C.S., F.R.C.O.G.

The Control of Chronic Alcoholism

QUERY.—Can you give advice on what can be done with the following patient?—A man aged thirty-six; a chronic alcoholic. He started drinking at the age of eighteen. There is a tendency for drink in the family. He has been in numerous homes for cure, but always discharged himself after a few days. He has seen several doctors and has had various treatments, without any lasting result. There are sober intervals for two or three weeks and then he becomes quite normal mentally and much improved physically. Does the law provide any means of control for this type of patient?

REPLY.—Unfortunately English law makes practically no provision for the drunkard who is a curse to himself and his family. If he is certifiably insane when comparatively sober he may be dealt with under the Lunacy Act, 1890; and if he behaves when drunk in some way which will bring him within the criminal law, e.g., by committing a serious assault or attempting suicide, he may be committed to an institution for inebriates. This, however, is hardly ever done and is of little use, because the drunkard is not likely to cooperate in his treatment. So far as the law is concerned the problem is insoluble.

D. HARCOURT KITCHIN
Barrister-at-Law.

PRACTICAL NOTES

A New Treatment for Headache

As a result of their experience with 100 consecutive patients with severe headache, J. W. Goldzieher and G. L. Popkin (*Journal of the American Medical Association*, May 11, 1946, **131**, 103) recommend the use of sodium nicotinate, given intravenously in doses equivalent to 100 mgm. of nicotinic acid. Seventy-five per cent. of the patients were completely relieved, including eight out of nine patients with migraine, thirteen patients with post-lumbar-puncture headache, five out of six patients with hypertensive headache, and 42 out of 53 patients with "idiopathic headache". Within thirty to forty-five seconds of the injection the patients complained of a sensation of heat in the genitalia, followed by a throbbing in the head and flushing. The relief of the headache corresponded with this peripheral flushing. Some patients also complained of paræsthesias, such as itching or pins and needles. The sensation of heat and the flushing usually subsided in fifteen to thirty minutes. In two patients mild abdominal cramps occurred, and in one vomiting. In thirty patients in whom the effect on the blood pressure was noted, no significant change was observed. As a control, thirteen patients were given an injection of 100 mgm. of nicotinamide, and in only three of these was there any relief of the headache, and this was only partial. In view of these preliminary observations, the authors recommend intravenous sodium nicotinate for the symptomatic treatment of (a) severe idiopathic headache, (b) migraine, and (c) the headache following lumbar puncture.

The Treatment of Epilepsy

PHENOBARBITONE, used alone or in combination with other drugs, is still the most useful anticonvulsant in the treatment of epilepsy, according to A. J. M. Butter (*Journal of Neurology, Neurosurgery and Psychiatry*, July-October 1945, **8**, 49). This conclusion is based upon an analysis of the results of treatment in 375 epileptic in-patients observed over periods varying from six months to five years. The criterion of treatment was an assessment of what drug or drugs appeared in each case to reduce the number of fits most successfully without obvious toxic reactions. The average dose in the case of both phenobarbitone and soluble phenytoin (epanutin) was 4½ grains (0.28 gm.) daily. Phenobarbitone used alone or in combination with other drugs was found to be the most successful form of treatment in 74 per cent. of cases, whilst soluble phenytoin, used alone or in combination with other drugs, was found to be the treatment of choice in only 23 per cent. of cases. Sodium bromide, again either alone or in combination with other drugs, occupied an intermediate position, being the most effective form of treatment in 40 per cent. of cases. At one time or another during the five-year period covered by this investigation, soluble phenytoin was given to practically half the patients, but in nearly 50 per cent. of these cases the drug was withdrawn, either because the efficient anticonvulsant dose produced toxic effects or because other drugs were found to be more effective in reducing the number of fits. It is pointed out that one reason for the poor results with soluble phenytoin in this series is the fact that it was withdrawn on the least evidence of toxicity, e.g., slight nausea or giddiness, persistent anorexia, or hypertrophic gingivitis causing any discomfort. Attention is drawn to the fact that with this drug toxic manifestations may develop, without increase of dosage, after a few days, a few months, or even after a few years.

The Ascorbic Acid Content of Human Milk

IN the spring and summer of 1942-43, Dora Winikoff (*Medical Journal of Australia*, February 1946, **33**, 205) carried out an investigation of the ascorbic acid content of the milk in a series of women from the lower and middle income groups in Melbourne. In nine samples examined, no evidence was obtained to support the view that the milk at the end of a feed is richer in ascorbic acid than that in the earlier stages, nor was there any difference in the milk obtained from the two breasts. An examination of 208 samples of milk in the colostral period in 186 mothers gave a range of ascorbic acid from 0.86 to 7.40 mgm. per cent., the mean value being 3.87 mgm. per cent. (standard deviation 1.45). An examination of 261 samples from 186 mothers, taken at monthly intervals during lactation, gave the following results : the ascorbic acid content ranged from 0.39 to 7.74 mgm. per cent., with a mean value of 3.67 mgm. per cent. The mean values for individual months rose slightly from the colostral period, remained constant during the first and second months, and then gradually fell, reaching the lowest level of 2.99 mgm. per cent. in the sixth month. Subsequently it rose. The differences between the third, fourth, fifth and sixth months as compared with the first two months were statistically significant. There was a significant fall in ascorbic acid content for colostral milk

October and for mature milk in November, nciding with the shortage of potatoes and sh vegetables. This investigation showed that to 60 per cent. of the breast-fed babies did t receive an adequate amount of vitamin C ring their first six months of life. It is there- e strongly recommended that breast-fed bies should receive some vitamin C supple- nt from the first few weeks of life.

ysuria in Heatstroke

EQUENCY of micturition is one of the well cognized early symptoms of heatstroke. . Kark (*South African Medical Journal*, arch 9, 1946, **20**, 111), however, has found at disturbances of micturition may sometimes the presenting feature of the condition. In e severe cases the other features of the ndrome overshadow the dysuria and diagnosis these cases is relatively easy, but in those ses in which dysuria is the presenting feature e true nature of the underlying condition may e overlooked. Thus, the patient may complain f painful urgency, delay in starting micturition, ain at the urethral meatus, and reduction in alibre of the stream with marked oliguria. In ddition there may be distressing and urgent alf-hourly frequency, straining and dribbling, æmaturia, and radiation of suprapubic pain o the loins. Details are given of one such case, een in India, where the patient was admitted to ospital with a diagnosis of urethral stricture, nd it was only after all urological investigations ad proved negative that the correct diagnosis of eat exhaustion was made. During a period of our weeks in India three other cases, two of hich had been diagnosed as "urethral stric- ure", and the other as "cystitis and urethritis", ere admitted to hospital and were found to be xamples of the pathological effects of heat. Therefore in the tropics the possibility of heat- stroke should be considered in any patient complaining of dysuria, even though the more characteristic features of the condition may not be present; these last may only be elicited on careful cross-examination of the patient.

Urinary Lithiasis

THE following data are culled from an analysis by H. P. Winsbury-White (*British Journal of Urology*, March 1946, **18**, 13) of 665 cases of urinary lithiasis he has seen during the last ten years. In 77 per cent. of the cases the calculi were in the upper urinary tract. Renal calculi were more common in males than in females (202 in males and 145 in females). This male preponderance is attributed to the fact that in the male the internal genital organs are more intimately related to the urinary tract

than in the female; hence infective processes in these organs would tend to encourage patho- logical processes in the kidney more easily in the male than in the female. Calculi were found in the left kidney in 160 cases, in the right in 120, and bilateral in 67. This preponderance in the left kidney is related to the fact that the testicular and ovarian veins on the left side enter directly into the renal vein, thus facilitating infection in this side from infective processes ascending from below in the perivenous lym- phatics. Of the total of 414 kidneys involved, 73 per cent. had a stone in the pelvis and, in many of these, stones were also found in the calyces. In 59 per cent. of the cases in which stones occurred in the calyces, these were localized in the lowest group of calyces. Ure- teric calculi showed a higher male incidence than renal calculi: 118 in males and 49 in females. As in the case of renal calculi they were more common in the left side: 93 in the left ureter and 67 in the right ureter. The most common site of impaction was outside the bladder, 55 occurring here whilst 18 were intramural. Nineteen were found in the lumbar region. Of the 132 vesical calculi, 115 occurred in males and 17 in females, whereas of the 19 urethral calculi, only one was in a female. This marked male preponderance is attributed to the greater tendency in the male for obstructive changes to occur at the neck of the bladder. In twelve cases the urethral calculi were associated with calculi elsewhere in the urinary tract. Of the 65 cases of prostatic calculi, 35 per cent. were associated with calculi elsewhere in the urinary tract.

Immunization against Whooping-Cough

USING a pertussis endotoxoid vaccine containing the antigenic qualities of phase I, *H. pertussis* organisms and the endotoxin, T. C. Brereton of Winnipeg (*Canadian Medical Association Jour- nal*, April 1946, **54**, 358) reports successful results in 436 children, aged four months to five years. Each child received four injections at fourteen days' intervals, the dosage being 1.0 c.cm., 1.5 c.cm., 1.5 c.cm., and 2.0 c.cm. The 6 c.cm. thus given to each child contained 90 billion phase I, *H. pertussis* organisms and 900 units of pertussis endotoxoid. No serious reactions were encountered, although in " one or two instances" the indurated area at the site of injection softened and ruptured. During a period extending over two-and-a-half years no case of pertussis occurred among the vaccinated children. During this period there were 1,171 cases of pertussis in Winnipeg, and this is calculated to correspond to a rate of 5.8 per

cent. among children under the age of seven years. The success obtained in this series is attributed to (1) the number of injections, (2) the interval between injections, and (3) the nature and unitage of the antigens that were used.

Procaine in Delayed Serum Sickness

DURING an investigation of the use of crystallized bovine albumin as a blood substitute, S. State and O. H. Wangensteen (*Journal of the American Medical Association*, April 13, 1946, **130**, 990) encountered a number of cases of delayed serum sickness which did not respond to the usual therapeutic measures, such as adrenaline. As some of these patients had severe pain in the muscles and joints, procaine was given to relieve this pain; not only was the pain relieved, but in addition the manifestations of serum sickness cleared rapidly. As a result of this experience, the effect of intravenous procaine was investigated in a series of cases. One gramme of procaine diluted with 500 c.cm. of isotonic solution of sodium chloride was given intravenously by the gravity drip method at a height of approximately 4 feet above the bed level over a period of two hours. If the injection is given more rapidly than this, flushing, dizziness and generalized numbness occur. A syringe containing amytal for intravenous administration was always available at the bedside to control any symptoms of sensitivity to procaine that might arise. No such symptoms occurred in any of the patients in this series. Of 16 patients with delayed serum sickness following bovine albumin solution, 10 obtained immediate and complete relief after one or more injections of procaine, four obtained temporary or partial relief, and two were unaffected. Immediate relief was also obtained in one patient with serum sickness following the injection of antitetanic serum. Of seven patients with urticaria, six obtained relief. One patient with asthma and one with rheumatoid arthritis showed no improvement, but one patient with status anginosus was free from attacks for three weeks following the intravenous injection of procaine. The mode of action in these cases is not at all clear, but in view of the marked response in the patient with status anginosus and the fact that a rise of skin temperature in the lower limbs occurred in four patients, it is suggested that intravenous procaine may be of value in the treatment of conditions associated with vasospasm or in Raynaud's disease.

Phthalylsulphathiazole in Operations on the Colon

AN intestinal antiseptic and bacteriostatic (phthalylsulphathiazole), which is stated to possess twice the bacteriostatic activity of succinylsulphathiazole, and is non-toxic, has been used in a series of fifty-one colonic operations, and the results are recorded by A. Thomson and E. M. Daland (*New England Journal of Medicine*, March 28, 1946, **234**, 431). The drug was also employed in the treatment of twelve cases of non-specific gastro-enteritis with diarrhœa, with apparent definite benefit. In cases of resection of a blind loop of the bowel or second-stage posterior excision of the rectum, daily pre-operative irrigations with phthalylsulphathiazole were given, but the routine procedure adopted was as follows:—Five or six days before operation phthalylsulphathiazole was given in initial dosage of 0.05 gm. per kgm. body weight (about 2.5 and 4.5 for most patients) and then 1 gm. (2 tablets) four-hourly, day and night. Enemas were given when required, but strong purges were not employed. Anæmia and low serum protein were corrected by the administration of whole blood, plasma, and amino-acid preparations. Twenty-four hours before operation clear liquids were given by mouth and routine doses of sulphadiazine, either orally or intravenously. In all cases except one, in which there was no obstruction, the bowel was found to be well cleaned and free from distention at operation. Determinations of the blood and urine levels of phthalylsulphathiazole were carried out daily, and in view of the low concentrations found and the complete absence of toxic symptoms, the more simple plan of giving all patients 1 gm. four-hourly after the initial dose, was adopted. In the series of fifty-one operations (forty-nine cases) the mortality rate was only 2 per cent.; wound infection was present in four cases, including the one fatal case, in which death was due to general peritonitis after a two-stage operation for carcinoma of the splenic flexure.

Functional Uterine Bleeding

USING the word "functional" bleeding to describe uterine bleeding when no disease of the uterus is present, M. C. Watson (*Canadian Medical Association Journal*, April 1946, 54, 342) divides such cases into two groups:—(1) Those cases in which the bleeding is the result of low continuous secretion of œstrogenic substances of the ovary, and in which the total period of sanguineous vaginal discharge, either in the form of spotting or active loss of blood, may be continuous for days or weeks, to disappear completely for a time and then to recur. In such cases the blood loss is rarely sufficient to cause secondary anæmia, which occurs only when the periods of bleeding are prolonged over weeks or months without intermission. (2) The

es in which the vaginal bleeding starts at or
ır the time of expected menstruation and
ıtinues beyond the normal period, the blood
s being sufficient to warrant the use of the
m "hæmorrhage," and the patient on
ımination showing evidence of secondary
ænia. The bleeding of the menopause is
t dealt with, the patients for whom the out-
e of treatment is given being those in whom
ə reproductive process is still active. In both
pes of case the possibility of malignant disease
ıst be eliminated: in type 1 cases curettage
ould be carried out as a diagnostic procedure
ıen the bleeding periods have recurred over a
riod of ten weeks, and the procedure is
sential in all type 2 cases when active measures
control the hæmorrhage are necessary. In
ıch cases curettage may assist therapeutically,
ıd especially when endometrial polypi are
moved. Hormone therapy in the form of
ʾ,000 to 20,000 I.U. œstradiol benzoate for
ʾe to seven days, followed by 5 to 10 mgm.
ʾogestin for two to four days may be employed
type 1 cases, but should never be employed
: type 2 cases, in which packing of the vagina
ʾr twenty-four to forty-eight hours is indicated
hen bleeding recurs after one curettage. Treat-
ıent in both types of case should be conserva-
ve in women under the age of thirty-five who
ʾe hopeful of future pregnancies, but in parous
ʾatients over the age of thirty-five who require
ʾo increase in their families, and when there is
efinite evidence of trauma of the cervix with
hronic infection and some enlargement of the
terus, hysterectomy with conservation of the
ʾealthy ovaries may be indicated.

Purpura and Pregnancy

ʾLTHOUGH thrombocytopenic purpura is not a
ʾommon complication of pregnancy (up to
ʾ944, sixty-two cases had been recorded), it
s accompanied by a maternal mortality of 55
ʾer cent., with a slightly higher infant mortality
ʾate. Reporting a case, W. B. Patterson (Journal
ʾf the American Medical Association, March 16,
ʾ946, 130, 700) draws attention to the salient
ʾeatures. In order to recognize purpura in
ʾregnancy before an acute attack occurs, the
ʾpossibility of its occurrence must be borne in
ʾmind in all pregnant women with a history of a
tendency to nosebleeds or bruising; those with
a history of post-partum hæmorrhage at a
previous delivery, and those with a family
history of "bleeders". As the serious conse-
quences are practically always due to post-
partum bleeding, all women with, or suspected
of having, purpura should be admitted to
hospital for delivery. Immediately after delivery
of the placenta the uterine cavity and vagina
should be firmly packed, and the pack left in
for twenty-four to thirty-six hours. Episiotomy
should be avoided. All infants born to mothers
with thrombocytopenic purpura should have
their blood typed immediately after birth, and
the bleeding time and blood platelets estimated.
Should bleeding or purpura occur in the infant,
treatment consists of repeated small transfusions
of blood. Patterson considers that proven
chronic thrombocytopenic purpura is a contra-
indication to pregnancy, but should an acute
attack occur in a hitherto normal woman who
is pregnant, there is little to be gained by
terminating the pregnancy.

The Nutritive Value of Beer

ACCORDING to Dr. F. W. Norris, of the Uni-
versity of Birmingham (Nature, April 6, 1946,
157, 430), beer contains about 3 per cent. of
carbohydrate, 0.2 per cent. of nitrogenous
substances and 3 per cent. of alcohol. The
carbohydrates consist of degradation products
of starch, but " there is no reason to suppose
that they are not digested in the normal
manner". The precise nature of the nitrogenous
substances is not known. The calorie value
ranges from 120 calories per pint for the mildest
ales to 400 calories per pint for the strongest.
but it must be remembered that this represents
the calorie or energy value and not the nutritive
value of the beer. "It is misleading and erro-
neous to confuse different foods solely on an
energy basis; all the nutrients in a food must be
compared when assessing nutritive value".
Of the mineral salts in beer, those of calcium are
the most important, ranging from 25 to 270
mgm. per pint. On the basis of a daily require-
ment of 800 mgm. of calcium, a pint of beer
would provide about 10 per cent. of this amount.
The calcium-phosphorus ratio equals unity,
but at the moment there is no evidence as to
how much of the calcium and phosphorus in
beer is absorbed by the body. Other salts in
beer include a small amount of copper and
manganese, as well as sodium chloride and
potassium salts. The vitamin B content con-
sists of 7-35 mgm. per pint of aneurin, although
as much as 85 mgm. has been found in some
strong ales; 200-800 mgm. per pint of riboflavin,
and 2-11 mgm. (average of 5-6) per pint of
nicotinic acid. The presence of the antiseptic
and other constituents of hops and the con-
ditions of manufacture "render beer, from the
microbiological point of view, one of the safest
of our beverages".

REVIEWS OF BOOKS

Injuries of the Knee Joint. By I. S. SMILLIE, O.B.E., M.B., F.R.C.S.ED., F.R.F.P.S. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. xi and 320. Figures 350. Price 35s.

THIS monograph covers a wide field and describes in detail the treatment of such varying conditions as supracondylar fractures of the femur and of the tibial platform, wounds of the knee joint and surrounding tissues, and injuries of the extensor apparatus, as well as giving a detailed account of the author's conception of the mechanism by which the varying injuries of ligament and semilunar cartilage are brought about, and the treatment which he advises. It is written as the result of his experience during the war years, when a vast amount of clinical material passed through his hands, which has been carefully analysed and studied. Mr. Smillie is to be congratulated on finding the time and energy for this detailed study. The most important section of the book deals with internal derangement—injuries to the semilunar cartilages. Here Mr. Smillie does well, once again, to emphasize the rôle of the quadriceps as the key to the functional use of the knee, and in the section on diagnosis to stress that a full and detailed "history" is of prime importance. There is an admirable chapter on the stiff knee, and another on injuries of the extensor apparatus, in which the advice given on the treatment of the fractured patella is sound. Some of the arguments and conclusions will not be generally accepted. Mr. Smiley's conception of the mechanism and his findings are not altogether in line with those which found general acceptance at the last full-dress discussion on injuries of the internal cartilage at the International Congress of Orthopædic Surgery in Rome in 1936. His primary transverse tear is difficult to follow and is denied by many surgeons of equal or greater experience. The operation for repair of a ruptured anterior crucial would require a long and careful follow-up of end-results before it could be accepted. At the present time there is much discussion on the training of a surgeon. Mr. Smillie's advice on page 291, that, "No surgeon who undertakes the treatment of fractures of the femur has completed his training until he has worked a shift at the coal face" might curb the enthusiasm of some aspirants. The book is beautifully produced and lavishly illustrated. There is no sign of austerity here, and indeed it is doubtful if some of the coloured plates are more effective than black and white—e.g., figure 10 "aspiration of hæmarthrosis", and figure 269, wrongly described as "backward displacement".

Morell Mackenzie. By R. SCOTT STEVENSON. London: William Heinemann (Medical Books) Ltd., 1946. Pp. viii and 194. Illustrated Price 15s.

MORELL MACKENZIE was one of the enigmas of the Victorian era, and in this fascinating book Mr. Scott Stevenson has amassed and sifted all the available information concerning the historic story of the fatal illness of Emperor Frederick III of Germany. Some men achieve notoriety, others have it thrust upon them. It is into this latter category that Morell Mackenzie fell when he was called to Berlin in 1887 to give an opinion upon the cause of the Emperor's hoarseness. For the next thirteen months he and his distinguished patient provided the headlines in the newspapers of two continents, and even to-day, sixty years later, there is no unanimity as to what the imperial patient suffered from or whether the case was mishandled by the man who was the leading laryngologist in the country. As an experienced laryngologist himself, Mr. Scott Stevenson is able to bring his professional knowledge to play upon the problem, and the unbiased reader will find it difficult to resist the case he makes out in favour of Morell Mackenzie. His considered opinion that the Emperor died of cancer of the larynx but the condition was anything but a typical case, and he does not exclude the possibility that the malignant change may have developed from a syphilitic lesion. This is a book that will appeal to all who are interested in the Victorian era, and it will have a particular appeal for medical men, for whom it would make an ideal present. The author is to be congratulated upon the skill with which he has performed a difficult task.

A Pocket Obstetrics. By ARTHUR C. BELL, M.B., B.S., F.R.C.S., M.R.C.O.G. London: J. & A. Churchill Ltd., 1946. Pp. 148. Figures 13. Price 7s. 6d.

IN a short foreword, the author points out that this book is intended to help midwives and general practitioners in their work, and students in their revision. In attempting to achieve this triple purpose, there has been perhaps some over-simplification of certain sections, but paragraphs dealing with such modern problems as the relation of the Rh factor to erythroblastosis fœtalis have been added. The work following closely the teaching of the Queen Charlotte's textbook, is orthodox in its arrangement, but such omissions as the hydrostatic reduction of the acutely inverted uterus, a description of the exact method of performing

pisiotomy, and mention of the Burns' manœuvre in breech delivery, are to be regretted. Mr. Bell is, however, to be congratulated on this short, clear and definite exposition of his subject, which should be of great value to those requiring a brief review of modern midwifery practice.

Sanitary Science Notes: A Handbook for Students. By H. HILL, F.R.SAN.I., F.S.I.A., A.M.I.S.E., and E. DODSWORTH, M.R.SAN.I., M.S.I.A. London: H. K. Lewis & Co. Ltd., 1946. Pp. 135. Price 7s. 6d.

IN this little book the authors of "Food Inspection Notes" deal with all subjects necessary for the student of sanitary science, but it should also be assured of a welcome from medical officers of health and sanitary inspectors. Although somewhat telegraphic in style the amount of information contained within the 128 pages of text is amazing; not only will the reader find up-to-date information on building construction, drainage, heating, ventilation, hospital, factory and school sanitation, sewage and refuse disposal, water supplies and the like, but sections are included on disinfectants, disinfection, household and insect pests, human parasites, infective and tropical diseases, and a number of other subjects. The book is a useful contribution to post-war scientific literature.

A Text Book of Forensic Pharmacy. By THOMAS DEWAR, PH.D., B.PHARM., B.SC., PH.C. London: Edward Arnold & Co., 1946. Pp. xvi and 253. Price 10s. 6d.

WRITTEN primarily for those studying for the qualifying examinations of the Pharmaceutical Society of Great Britain, this book should also make a wide appeal to general practitioners, and particularly to those interested in forensic medicine. Poisons and dangerous drugs, and the law pertaining thereto, are discussed in detail, and the Poisons List and Poisons Rule, 1935, are given in full in the appendices. Appendix F is devoted to the National Health Insurance (Medical Benefit) Regulations, 1936-45. Practitioners will find much useful information in the chapter on the Food and Drugs Act, and in the chapter on medicinal dangerous drugs. The revision questions given in Appendix G, which include examples of those set in the qualifying examinations of the Pharmaceutical Society of Great Britain, should be of considerable assistance to students.

NEW EDITIONS

IN the second edition of the popular textbook *Cardiovascular Disease in General Practice*, by C. F. TERENCE EAST, D.M., F.R.C.P. (H. K. Lewis & Co. Ltd., 12s. 6d.), the author, unlike many, has managed to carry out radical revision without at the same time increasing the size of the book. One of the outstanding features of this book is the complete absence of electrocardiograms: a deliberate omission on the author's part, and one for which there is much to be said. Intensely practical in its outlook, this is a book that will commend itself to the general practitioner, but it does lend itself to criticism in places. For instance, although the author takes the utmost care to state, with admirable impartiality, the pros and cons of tobacco in heart disease, he does not mention the only really valid objection to its use in heart disease, namely its liability to cause unnecessary coughing. The attempt to be brief has led to considerable confusion in the paragraph on Addison's disease, and it is disturbing to find heparin dismissed so lightly in the treatment of thrombophlebitis. It is surprising to find no reference to the newer sympathomimetic drugs in the treatment of circulatory failure during anæsthesia. These, however, are minor blemishes in a book which the practitioner will find most valuable in his daily round.

THE second edition of *The Chemical Composition of Foods*, by R. A. McCANCE and E. M. WIDDOWSON (Med. Res. Coun. Spec. Rep. Ser. No. 235, H.M. Stationery Office, 6s.), contains data relating to a number of new foods the compositions of which have been investigated since the publication of the previous edition. The recipes included in the new edition, which are adapted to the use of post-war materials, will be warmly welcomed. Although the form of the main tables has not been changed, a number of additions add considerably to their value for present-day use.

A Complete Outline of Fractures, by J. GRANT BONNIN, M.B., B.S., F.R.C.S., in its second edition (William Heinemann (Medical Books) Ltd., 30s.) has been largely rewritten. A considerable amount of new material has been added, and many illustrations, the total number of which is now 712. Sections are included on the chemotherapy of wounds, and on the use of penicillin and proflavine. There is a most useful chapter on plaster technique, and Mr. J. N. BARRON, F.R.C.S.ED., has collaborated in rewriting the chapter on fractures of the face and jaw. Although the book is written primarily for the student, practitioners will find it a useful addition to their armamentarium.

NOTES AND PREPARATIONS

NEW PREPARATIONS

BENADRYL (β-dimethylaminoethyl benzhydryl ether hydrochloride) is a new synthetic compound stated to be both anti-allergic and anti-spasmodic, thus being capable of antagonizing the action of histamine and affording relief in a number of allergic conditions. Benadryl is administered orally and, in responsive cases, it exerts a beneficial effect within a few hours. Successful results have been reported in hay fever and urticaria. Side-effects, such as transitory drowsiness, are not common and are easily controlled. Benadryl, which is issued in bottles of 50 capsules each containing 50 mgm., is marketed by Parke, Davis and Co., Ltd,. 50 Beak Street, Regent Street, London, W.1. Supplies at present are strictly limited.

EVANS DERMAL POWDER (E.D.P.) is a mixture of bismuth subiodide, thymol iodide and formalized gelatin combined with magnesium borate and magnesium stearate. Indications for the use of this surgical powder, which is stated to have absorbent, deodorant, disinfectant and mildly astringent properties, are as a soothing dressing to wounds, chafing, sunburn, insect bites, and as a deodorant in hyperidrosis. E.D.P. is available in sprinkler tins of 2 ounces, price 2s., hospital size, 6s. 8d. The manufacturers are Evans Medical Supplies Ltd., 50 Bartholomew Close, London, E.C.1.

SUCCINYLSULPHATHIAZOLE M. & B.—This member of the sulphonamide group of drugs is stated to be of low toxicity, as the degree of absorption (5 per cent. or less of the amount ingested) is low. Its use is indicated in the treatment and prevention of bacillary dysentery, and it is stated to be effective not only in Shiga and Flexner infections but also in Sonne infection. In surgery, succinylsulphathiazole can be used both pre- and post-operatively for the prevention of peritonitis, fæcal fistulæ and wound infection in operations on the rectum and colon. Succinylsulphathiazole M. & B. is issued in tablets of 0.5 gm., in containers of 100 and 500, by May & Baker Ltd., Dagenham, Essex, from whom an explanatory booklet can be obtained.

ROYAL MEDICAL BENEVOLENT FUND

AT the Annual General Meeting of the Royal Medical Benevolent Fund, held on June 12, the President, Sir Arnold Lawson, K.B.E., F.R.C.S., referred among other things to the plans in progress for the purchase of a house on Putney Hill to provide a home for aged members of the medical profession. The house in question will accommodate about a dozen beneficiaries,

each of whom will have a private bed-sitting room as well as the use of a communal sitting and dining room. The rentals will be low and no-one will be excluded on financial grounds. If the original effort proves a success it is proposed to extend the scheme to houses for married couples or single people of both sexes. Funds, of course, will be required—in the President's own words: "to carry out the complete scheme . . . it is going to cost a very great deal of money, and how much we can enlarge it . . . depends upon the generous support of our medical colleagues". The Honorary Treasurer of the Fund is Dr. C. Luther Batteson, the Secretary Mr. E. C. Pennefather, M.B.E., 1 Balliol House, Manor Fields, London, S.W. 15.

"THE SILENT WORLD"

THE first number of The Silent World, the official journal of the National Institute for the Deaf, was issued in June 1946. One of the aims of the journal, as stated by the Duke of Montrose in his opening message, is to put the deaf and dumb across to the hearing, and no less to bring the hearing across to them. All topics are dealt with—books, entertainments, holidays, sports—and there is a most interesting article on the Mary Hare Grammar School. The journal is published monthly, price 6d. per copy. Communications should be addressed to the Editor, The Silent World, 16 Woodfield Road, Welwyn Garden City, Herts.

THE BRITISH LEGION UNIT OF RHEUMATOLOGY

THE one-year scheme initiated by the British Legion Unit of Rheumatology has already begun its work at the Three Counties Emergency Hospital, Arlesey, Beds. The patients, all ex-Service men and women, are resident in the hospital and after accurate basic diagnosis, treatment is instituted under the supervision of consulting specialists in rheumatology. Lord Horder is the Consultant Observer. A rehabilitation supervisor has been appointed under whom a steady progress towards working capacity is made. The Joint Council of St. John and the British Red Cross Society provide a ferry service so that contact with friends and relations may be kept alive and active.

MEDICAL AUXILIARY SERVICES: SPEECH THERAPISTS

THE fourth edition of the National Register of Speech Therapists (1945-46) has just been published by the Board of Registration of Medical Auxiliaries. Copies can be obtained free on application to the Registrar, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, London, W.C.1.

RECENT TRENDS IN THE INCIDENCE OF INFECTIVE FEVERS

By W. H. BRADLEY, D.M.

Senior Medical Officer, Ministry of Health.

LOOKING back over the war years to the dark days of 1939 it is somewhat amusing to recall the atmosphere of pessimism braced with high resolve which arose because it was believed that with war must come pestilence. Pestilence did not come and in this respect history failed to repeat itself. Although as yet there has hardly been time to inquire into the reasons for this remarkable deliverance the facts are now available (Sir Wilson Jameson, 1946*) and it is convenient to discuss the trends in the incidence of the infective fevers during the war years. It is convenient, but not necessarily safe, to choose this period. Trends are significant only when observed over periods of time sufficiently long for the purpose of the observation. At the peak of a localized outbreak of disease, or in a pandemic, for example of influenza, the change in incidence from week to week may have a profound meaning, but in the appraisal of the effect of a preventive measure ten years may be too short a period. However, for the purpose of bringing into perspective the relative importance at the present time of the several infective fevers the figures given in this account are safe.

In assessing the importance of a disease it is not sufficient to know only the incidence as ascertained by notification. No matter how deep may be concern about the time lost, the cost of hospital treatment, the crippling and maiming and the chronic invalidism resulting from a disease, the ultimate criterion of importance is the mortality.

GENERAL TRENDS

Deaths from all the infective diseases included in the International List of Causes of Death (No. 1-44) totalled 34,125 in 1945*. This was 1,731 fewer than in 1944; 9,798 fewer than in 1939 and 13,466 fewer than in 1943, but in this year influenza caused 12,616 deaths as compared with 2,686 in 1945. This most encouraging balance sheet is still more satisfactory when con-

---

*"On the State of the Public Health during Six Years of War". Report of the C.M.O., Ministry of Health, 1939/45, H.M. Stationery Office, 1946. Figures in tables 1 and 3 have been taken from this Report. Figures for 1945 come from another source: they are only provisional.

TABLE I

NOTIFICATIONS AND/OR DEATHS IN EACH YEAR 1938-1944 INCLUDING NON-CIVILIANS, ENGLAND AND WALES

		1938	1939	1940	1941	1942	1943	1944
Pneumonia, acute primary and influenzal ..	Notifications	45160	42312	47875	50942	42698	52407	38631
	Deaths	29646	26991	33903	29298	22217	30339	21723
Influenza ..	*Deaths*	4446	8020	11482	6901	3399	12616	3900
Diphtheria ..	Notifications	65008	47343	46281	50797	41404	34662	23199
	Deaths	2861	2133	2480	2641	1827	1371	934
Whooping-cough ..	Notifications	?	?	53617	173330	66016	96136	94044
	Deaths	1052	1229	678	2383	799	1114	1054
Measles ..	Notifications	?	?	409521	409715	286341	376104	158479
	Deaths	1524	303	857	1145	458	773	243
Cerebrospinal fever ..	Notifications	1288	1500	12771	11077	6029	3303	2309
	Deaths	655	517	2584	2163	1206	780	592
Dysentery, all forms ..	Notifications	4170	1941	2860	6670	7296	7905	13025
	Deaths	112	96	185	329	198	124	157
Scarlet fever ..	Notifications	99278	78101	65302	59433	85084	116034	92671
	Deaths	311	181	154	133	104	134	107
Poliomyelitis and polioencephalitis	Notifications	1585	831	1079	959	674	456	532
	Deaths	256	143	161	160	132	90	109
Typhoid and paratyphoid fevers ..	Notifications	1322	1479	2833	4763	858	713	542
	Deaths	159	112	135	148	89	72	55

sidered in conjunction with the figures over a longer period of time, but these are best appreciated when individual diseases, or groups of diseases are discussed. This will·be done in the order, roughly, of the importance of the disease entity as a potential source of pestilence. Tuberculosis will not be included.

TABLE 2

FIGURES (PROVISIONAL) SHOWING TREND OF MORTALITY RATE COMPARING 1945 WITH 1939

Downwards			Upwards		
	1945 Deaths	Fall compared with 1939	·	1945 Deaths	Rise compared with 1939
Influenza	2686	5334	Measles ..	729	426
Diphtheria	720	1413	Dysentery,		
Whooping-cough ..	689·	540	all forms	165	69
Acute poliomyelitis and			Cerebrospinal		
polioencephalitis ..	139	4	fever ..	555	38
Scarlet fever	84	97			
Typhoid fever ..	32	58			
Paratyphoid fever ..	15	7			

TYPHUS FEVER

The only cases of epidemic (louse-borne) typhus encountered in England and Wales were imported from the Continent, mainly in repatriated prisoners of war, and numbered less than two dozen. In no case was there evidence of lousiness at the time of importation—a remarkable tribute to the efficiency of the precautions taken by the fighting Services. The threat was considerable because the disease appeared in a hundred different foci in the British Zone of Germany alone between the end of hostilities and the beginning of 1946, but on each occasion the delousing of contacts with D.D.T. resulted in speedy termination.

SMALLPOX

It is not always realized that a fundamental change occurred in the circumstances of these Islands when a decade ago variola ceased to be endemic here. Unless the situation is changing at this moment there is no risk until the disease is newly introduced. Opportunities for introduction have unfortunately been numerous of late; cases have been imported on a score of different ships repatriating troops from India and the East during the first half of 1946, and on a few occasions alarming situations arose when secondary cases occurred, but control has been obtained with remarkable speed by the vaccination and surveillance of contacts.

ENTERIC FEVERS

In 1944 and 1945 deaths from enteric fever fell below one in a million of the population. In the four decennial periods 1871 to 1910 they were 321, 199,

175, and 91 per million respectively, since when the decline has approached arithmetical progression (see table 3). So dramatic a trend might give a false sense of security. Unfortunately, in certain respects the present position is not entirely satisfactory and it would be better to accept the present low figures as a challenge calling for a determined effort to eliminate enteric fever from these Islands. The unsatisfactory features are:—First, there has been no reduction whatever in the case fatality. Secondly, typhoid and paratyphoid fevers are still widely endemic. In recent years, most of the cases notified have been sporadic, and the present low figures represent small foci which have failed to give rise to sizeable epidemics. Thirdly, since the first flush of success which followed improvement in sanitation and water supplies the decline has resulted mainly from (a) improvement in food handling habits, (b) pasteurization of milk, (c) the multiple shop catering organizations using well-controlled kitchens and (d) the development of food combines and mass distribution serving wide areas of the country. Food handling habits should continue to improve, but in respect of the guard against the introduction of typhoid and paratyphoid infection into widely distributed aliments the great machines (b), (c) and (d) are not exempt from breakdown, and explosive, even devastating, outbreaks of enteric fever are still possible. The position is vastly different from that of smallpox, which is no longer endemic, for typhoid carriers are numerous and are always a potent danger. However, the problem is now of tangible proportions, and recent advances in bacteriology have provided ways and means for studying and reducing the endemicity.

DYSENTERY AND OTHER ALIMENTARY INFECTIONS

Although not strictly in order of precedence, this group can most conveniently be discussed at this point. The actual figures have, to some extent, been influenced by a change in the habits of practitioners who are beginning to realize that dysentery is notifiable under the Public Health (Pneumonia, Malaria, Dysentery, etc.) Regulations, 1919.

During the past ten years there has been at least a tenfold increase, and in 1937 to 1938, and again in 1941 et seq, B. dysenteriæ sonne became a pathogen of major importance. This prevalence has been particularly disquieting because the Food and Drug Act of 1938 and a considerable amount of propaganda directed towards improved food handling and personal hygiene have had no apparent effect. There are now large numbers of symptomless carriers in the population and patients may continue to excrete the organism for many weeks.

The same may be said of the salmonellæ. Characteristic outbreaks of food poisoning and much sporadic diarrhœa and vomiting resulted from imperfect cooking of imported dried egg contaminated in bulk and at source, but since the cessation of lease-lend eliminated the dried egg hazard Salmonella typhi murium (ærtrycke) has shown signs of active spread and may well

assume the position once held by *B. paratyphoid* and recently contested by *B. sonne*. Even so, dysentery and salmonella infections account for a small proportion only of the alimentary upsets which have become quite a feature in this country of late. "Epidemic nausea and vomiting", a characteristic clinical state of unknown origin, was prevalent in 1943 and 1944, and early in 1946 a non-bacterial diarrhœa, sometimes with fever, and apparently distinguishable from epidemic nausea and vomiting, swept through the country. The probability is that these novelties, whether newly introduced or merely newly recognized, are of virus origin. Although pertinent information concerning the etiology of "gastric flu" must come from the virologists, more complete clinical and ecological descriptions are the first requirement.

INFLUENZA

Deaths certified as due to influenza include a high proportion of deaths due to fevers of unknown origin, many of them infective, and in years when there is no laboratory evidence of the presence in a big way of influenza virus, thousands of deaths are attributed to this cause, probably wrongly, but for want of a better name and classification. True epidemic years have been 1933, 1937, 1940 and 1943. The last devastating wave was in 1929, yet including this and all subsequent years together the total score of deaths is no greater than occurred during the 1918/19 pandemic. The gloomy expectation that the present peace might bring again the catastrophic disease which followed world war I has not yet been fulfilled. The 1946 virus B outbreak was mild and sporadic. Some parts of England and Wales were hardly affected at all, and deaths were substantially less than in the virus A wave of 1943. The forecast is not so good, for since 1933 epidemic proportions have been reached every three or four years, and we are approaching the danger point in another cycle.

RESPIRATORY INFECTIONS

Pneumonia.—It is not customary to classify pneumonia with the infective fevers mainly because the diagnosis when used as a certified cause of death includes a multiplicate of disease entities. Of these, pneumococcal lobar pneumonia is no less a communicable disease than is scarlet fever, and the trends in incidence are interesting when considered with those of the streptococcal diseases. The deaths from lobar pneumonia have been:—

1939	1940	1941	1942	1943	1944	1945
6977	7271	7117	5933	6534	5364	4955

It is difficult to read into these figures a clear reflection of the influenza outbreaks of 1940 and 1943 and, in fact, those who watch trends in the hope of being able to forecast and prognosticate the behaviour of influenza are sorely disappointed with the help they get from pneumonia notifications and

death certification. In 1946, pneumonia notifications did not show a significant rise over 1945 in most weeks during the influenza epidemic.

The value of sulphonamides in the treatment of lobar pneumonia is not questioned, and it is true that since their introduction lobar pneumonia in its classical form has been seen much less frequently. It is equally true that the downward trend in deaths from pneumonia was apparent before sulphonamides were introduced, and that in the past seven years there has been no dramatic speed-up in the decline. Commensurate trends have occurred in the death rate from typhoid and tuberculosis, the causal organisms of which are not sulphonamide-sensitive. These are shown in table 3 which, for another reason, also includes rheumatic fever and heart disease.

TABLE 3
DEATH RATE PER MILLION LIVING

Year	Pneumonia (all forms)	Tuberculosis (respiratory)	Typhoid fever	At ages under 15 years		
				Scarlet fever	Rheumatic fever	Heart disease
1911-15 ..	1103	1005	47	185	57	137
1916-20 ..	1192	1009	22	96	52	115
1921-25 ..	974	815	12	91	57	101
1926-30 ..	898	721	9	55	57	88
1931-35 ..	766	601	5	50	46	84
1936 ..	683	509	6	38	44	75
1937 .	710	508	5	27	34	67
1938 ..	637	463	4	27	44	68
1939 ..	513	463	2	15	34	56
1940 ..	661	538	3	12	30	49
1941 ..	619	571	4	11	22	45
1942 ..	470	524	2	9	18	39
1943 ..	542	549	2	11	27	40
1944 ..	430	528	1	9	28	42

STREPTOCOCCAL DISEASE

Eighty years ago *scarlet fever* killed more children under fifteen than did respiratory tuberculosis at all ages. The death rate in the decade 1861-70 was 2,617. In 1944 it had fallen to 9 and to still less in 1945. Scarlet fever is no longer a major hazard and florid cases are rarely seen these days. This remarkable decrease in the damage done by Dick toxin is another of those surprising epidemiological trends which "just happen" in the history of the world. Minor reverses in the trend occur from time to time, as instanced by the doubling of notifications between 1941 and 1943. This rise occurred in spite of enthusiastic and sometimes indiscriminate use of sulphonamides. The rise might have been more dramatic had sulphonamides not been used, but American experience in recent years puts a different complexion on the case. There, three different sulphonamide-resistant types of *Streptococcus pyogenes* appeared as out of the blue and spread widely throughout the United States, causing a very considerable epidemic of scarlet fever in spite of deliberate chemo-prophylaxis in some of the localities involved.

The trends in other clinical states largely associated with streptococcal infection are shown below (table 4).

TABLE 4

		1939	1940	1941	1942	1943	1944	1945
Erysipelas	Notifications	14141	13123	12232	11598	11833	11148	
	Deaths	248	214	190	141	124	119	119
Purulent in-fections and septicæmia	*Deaths*	487	518	477	411	394	407	301
Puerperal pyrexia	Notifications	9252	7627	7356	8542	8354	7944	
Diseases of the ear and mastoid ..	*Deaths*	1189	1009	912	928	1080	1016	908

There was little or no reduction in the overall incidence throughout the war years, but fatality is lower. The striking parallelism between the figures for scarlet fever and rheumatic fever and heart disease, when viewed over the past thirty years, is interesting (table 3).

CEREBROSPINAL FEVER

The behaviour of this disease, the epidemiology of which is much the same as in pneumonia and scarlet fever, has been disturbing. Since an eightfold rise in 1940 compared with 1939, there has been a decline, but 1939 figures have not yet been reached. Deaths per million are still about twice the figure for 1921 to 1925, when they were 11. During the epidemic of 1940 to 1941 they were 79 and 66 respectively. It has not always been realized that the death rate from cerebrospinal fever per million living has been twice as great during this war as it was during world war I, and this in spite of sulphonamides, which undoubtedly brought about a four- or five-fold reduction in case fatality.

DIPHTHERIA

Unlike scarlet fever, diphtheria had not declined in the ten years before the war, and in the quinquennium 1931 to 1935 it was the principal killing disease at school age. The recent downward trend, undeniably resulting from immunization, has been obtained against considerable odds, because at the same time a serious epidemic has occurred in Europe where, as well as in North Africa during the campaigns, British and American troops were affected and frequent opportunities for the introduction of the disease into these Islands must have occurred. Occasionally, of late, a sudden change in the type of *C. diphtheriæ* has been noticed at the beginning of a period of *increased prevalence in certain localities*, suggesting that a new organism of

high virulence has been introduced. In these circumstances the disease has spread and involved immunized persons.

In general terms, the estimated position with regard to diphtheria immunization is that 58 per cent. of children under fifteen are immunized and that of every 30 deaths in 1945, 29 occurred in unimmunized persons. A striking feature of diphtheria during the past ten years has been a relative increase in the number of adults attacked. During 1945, one in every three cases and one in every six deaths occurred in persons over fifteen years of age.

WHOOPING-COUGH

Whooping-cough has been killing more children than measles during the war, and in 1941 deaths from this cause were higher than in any of the ten preceding years. Fortunately, there was a rapid decline in 1945, but notifications are now mounting again. The case fatality, which does not appear to change, is the most alarming feature. At ages up to two, whooping-cough kills more than diphtheria and half the total deaths are of children under the age of one year. The development of an efficient prophylaxis is a hard-felt want and in the matter of therapy whooping-cough deserves more attention than any other of the common communicable diseases of childhood.

MEASLES

Since an attack of measles during the first decade of life is almost inevitable, trends in incidence have little significance. The biennial periodicity of this disease is well known. Evacuation appeared to disturb the cycle and to postpone the peak expected in 1940 until 1941. Since then, the biennial rhythm has returned and the coming winter should be an epidemic season. The anticipated rise in notifications had already begun by midsummer, 1946.

An encouraging feature is the low fatality rates (under 0.3 per cent.) observed during the war years. A similar decline in fatality has also been noticed in the United States. It is conceivable that these low rates are associated with the decline in the incidence of the micrococcal infections which have in the past played a major rôle in death from measles.

POLIOMYELITIS AND POLIOENCEPHALITIS

Deaths, which decreased in 1943/44, rose to 1939 level again in 1945; of late, notifications of poliomyelitis have continued to increase over the 1945 figure. At midsummer, 1946, when this article was written, this upward trend, preceding the season when poliomyelitis has its greatest incidence, is an adverse sign. Cases are, for the most part, sporadic, but localized outbreaks must be anticipated this autumn. Poliomyelitis has never become truly epidemic in this country although there have at times been signs suggesting a widespread parisitism. The forecast is not unduly gloomy because the population appears to have a nicely balanced immunity, and

there is no reason why it should break down in a large way. It is interesting to note that during the war the more spectacular and explosive outbreaks occurred in remote communities, the main examples being Malta, Mauritius and St. Helena.

OTHER DISEASES

There have been upward movements in certain diseases not ordinarily included with the infective fevers, but which are probably communicable. As a cause of death, *hepatitis* is now of greater importance than scarlet fever or dysentery. *Hodgkin's disease* killed 652 in 1945, an increase of 123 over 1939. Deaths from *enteritis* and *diarrhœa* at ages under two years continued to rise and numbered 377 in 1945. Non-bacterial diarrhœa in the newborn was an outstanding problem.

CONCLUSION

Although guard against plague, typhus, yellow fever, smallpox, relapsing fever, cholera and typhoid, must never be relaxed, these are now of little moment in these Islands. The main enemies amongst the communicable diseases are tuberculosis, influenza and the great group of respiratory infections. Downward trends in pneumococcal and streptococcal disease which anticipated chemotherapy are to some extent offset by a prevalence of cerebrospinal fever in spite of chemotherapy.

There is uneasiness concerning poliomyelitis this autumn. A wave of measles is expected this winter and the whooping-cough incidence appears to be rising. If the present position with regard to diphtheria is to be held there must be more immunization. No spectacular new disease emerged during the war, but gastro-intestinal upsets have become disturbingly frequent. Some of these are believed to be due to filter-passing infections which are at present unidentified, but which do not appear to be food-borne.

On the whole there is a good hold on those infective fevers about which most is known, but anxiety is felt concerning the virus diseases and the fevers of unknown origin. Although it would be vain to deny that natural forces beyond the control of man have determined this position, man's influence is obvious and in proportion to his knowledge. Reconnaissance is a prerequisite of good preventive measures and in this all practitioners can assist: whilst they may not feel impelled to take an active part in the "selfless search after truth" they still can make a contribution by exercising care in the notification of infective disease and the certification of death and by consulting with the Public Health officers whenever they suspect infection.

PROPHYLAXIS IN SOME COMMON FEVERS

By E. H. R. HARRIES, M.D., F.R.C.P.

Medical Superintendent, North Eastern Hospital, London County Council.

IT is proposed to discuss prophylaxis in the four major common fevers of childhood. Arranged in order of their current importance these are whooping-cough, measles, diphtheria and scarlet fever (Cruickshank, 1943), but for convenience of description this order of precedence will be reversed and the diseases arranged in two pairs, each of which has etiological and epidemiological similarities, namely, diphtheria and scarlet fever, measles and whooping-cough. Their main characteristics may be briefly recalled.

DIPHTHERIA AND SCARLET FEVER

Diphtheria is primarily an infection of the nasopharyngeal mucosa with the *gravis, intermedius* or *mitis* strain of the *C. diphtheriæ*. With the exception of the laryngeal form, which is nearly always an extension from a primary faucial or, in infants, post-nasal focus, the danger in diphtheria is due solely to the dissemination from the locus of infection of an exotoxin which is quickly fixed in all the tissues, with possibly disastrous results upon those of the circulatory and nervous systems. Although relatively uncommon among infants under one year of age, diphtheria is then most fatal because of the greater liability to laryngeal obstruction.

Scarlet fever.—The syndrome scarlet fever is one of the hæmolytic streptococcal fevers and is primarily an infection of the nasopharyngeal mucosa with beta-hæmolytic strains of the *Str. pyogenes*. The strains associated with the syndrome produce, in varying degree, an erythrogenic toxin, to the dissemination and fixation of which the rash, if it occurs, and other manifestations of toxæmia are due. But the causal organism has invasive properties and there may thus be superimposed upon the clinical picture of tonsillitis (the essential factor) and a rash (an inconstant epiphenomenon), local or general manifestations of sepsis. Scarlet fever has for many years been so mild that death is most unlikely; its chief importance arises from the undoubted but unexplained association with rheumatism, and from the large contribution the hæmolytic streptococcus makes (as in measles) to the national problem of deafness.

MEASLES AND WHOOPING-COUGH

The virus of *measles* ranges widely in the tissues and can in the early stages of the attack be recovered from the nasal secretions and the blood. Although highly infective in the earliest pre-exanthematous (Koplik's spots) stage, the virus soon disappears, and by the time the rash has faded the patient, *qua* measles, has ceased to be infective. But the real menace of measles to the very young child arises not so much from the virus as from secondary invaders, hæmolytic streptococci in particular, of the upper and lower respiratory mucosa, the resistance of which is lowered as the result of the

activities of the virus. Broncho-pneumonia, if it does not kill so frequently as in the past, may yet result in fibroid lung and bronchiectasis; and middle-ear disease in deafness or deaf-mutism. Whereas measles rarely attacks infants under three months old and is, to some extent, modified in those up to six or eight months of age, the child of a few weeks old may suffer a typical and severe attack of *whooping-cough*—undoubtedly on all counts the most formidable of the common acute specific fevers of childhood.

H. pertussis invades the pharyngeal and tracheal mucosa, causing an initial and highly infective catarrhal stage which merges into a paroxysmal stage of steadily decreasing infectivity; the causal organism is recoverable only in a small minority of cases when this stage has endured for a month, although the paroxysms may still persist for many weeks. The paroxysmal stage of pertussis, like the exanthem of scarlet fever, is an inconstant epi-phenomenon and is caused, or believed to be caused, by an endoneurotoxin, elaborated by the organism during the catarrhal stage of the attack. This toxin sensitizes to respiratory stimuli the sensory nerve-endings in the invaded mucosa, and the paroxysms are the result of such stimuli. Although a greater menace to infant life in its own right, so to speak, than measles, because of the earlier age at which attack may occur, the liability of the infant to convulsions, and the long debilitating illness, whooping-cough, like measles, is chiefly formidable by virtue of the frequency with which second-ary invaders cause broncho-pneumonia.

From the epidemiological aspect these four fevers have several features in common; all are primarily endemic infections of the upper or lower respira-tory tract and are transmitted by droplets through distances of .three to four feet or, especially in measles, by droplet nuclei which may be air-borne over longer distances (Cruickshank, 1940); all exhibit at more or less regular intervals local or general epidemic prevalence; and all are essentially "school" diseases contracted first by non-immunes of school age and transmitted by them to younger children at home.

GENERAL PROPHYLACTIC MEASURES

Prophylaxis in the infective diseases includes any measures tending to reduce incidence or, failing this, to mitigate the severity of an attack should it occur.

(1) *Environment and nutrition.*—The importance of environment as a factor in the prophylaxis of infection, whether general or specific, has been stressed in numerous medico-social studies. The best environment will not, of course, prevent the introduction of infection to the household, but that good environment does exert a favourable influence upon the *results* of infection there is abundant evidence to show. Measles, for example, in the tenements of the poor is very different from measles in the nurseries or public schools of the well-to-do. Halliday (1928) showed that the better the environment the later the age at which attack occurred and the lower the incidence of, and deaths from, concomitant broncho-pneumonia. Cruickshank (1945) points

out that exogenous infections like measles and pertussis are as common among well-fed as among ill-fed children, and yet in the age-group of one to two years deaths from measles are eighteen times more common in the lowest than in the highest social class, among whom resistance is greater. What is true of measles is also true of the other diseases (Gale, 1945).

(2) *Isolation.*—Isolation of the patient who is even suspected to be a source of infection is obviously an essential step to be instituted at the earliest possible moment and enforced until bacteriological evidence or clinical experience, or both as the case may be, justify its termination. Yet, as a communal measure isolation has failed to reduce the prevalence of the group of fevers under discussion. Endemicity of diphtheria and scarlet fever is maintained not by the minority of patients who develop clinically recognizable and therefore isolated attacks, but by the far more numerous subjects of atypical attacks and subclinical infections, and by those who are either contact or convalescent carriers.

Whooping-cough and measles have been hospitalized upon any considerable scale only during comparatively recent years, and then admittedly not as a measure of control but upon social and therapeutic grounds. Lightly regarded by the public, medical advice is sought for these two diseases only when the attack is well advanced and the contacts have already been infected.

(3) *Quarantine and school closure.*—At one time it was common practice upon the outbreak of one of these diseases, particularly measles, to subject the contacts to a period of exclusion or "quarantine" and to close the school. Both these measures were ineffective and have disappeared, or virtually disappeared, in favour of the exclusion of suspects or actual victims and the daily surveillance of contacts.

THE RÔLE OF THE BACTERIOLOGIST

In diphtheria, scarlet fever and whooping-cough, the bacteriologist plays an important prophylactic rôle.

DIPHTHERIA.—It is true that in diphtheria diagnosis has too often been permitted to await the report upon a swabbing, to the detriment of the patient and the contacts but, provided that the precautionary measures of isolation and antitoxic therapy have been instituted, even upon suspicion, (the bacteriological report being regarded as a confirmatory diagnostic procedure), the taking of a swab is a wise precautionary measure. The main usefulness of the swab in diphtheria, however, lies in the detection of carriers. The bacteriologist alone can determine whether the patient, convalescent after an attack of diphtheria, is still a source of infection or not, and his aid is essential in tracing carriers in an institutional outbreak. Swabbing combined with Schick tests will result in the detection of the dangerous immunes carrying a virulent strain of *C. diphtheriæ*. By plating on tellurite media the skilled bacteriologist can determine the strain on inspection of the colony morphology after incubation, and thereby the virulence of the organism; gravis and intermedius strains are almost invariably virulent, but some 10 per cent. of mitis strains are non-virulent and

may therefore require further investigation. Whether for confirmation of diagnosis or detection of carriers, swabbings should always be procured from throat *and* nose, and the fullest information as to the source should always accompany the swabs to the laboratory.

Bacteriological clearance.—Whether the carrier is "convalescent" or "contact" it is customary to obtain three consecutive negative reports upon swabbings from throat and nose prior to release from isolation; at least three days should intervene between the swabbings, and no antiseptic gargle or spray should have been employed for at least twenty-four hours before the swabbing. Discussion of the management of the diphtheria carrier in any detail is beyond the scope of this article. Most persistent carriers have some abnormality of the nasopharyngeal mucosa and this should be noted as soon as possible, but in my opinion surgical procedures should be resorted to only when other methods have proved unsuccessful. It is essential to secure for the carrier an abundance of fresh air and this measure alone may effect a cure. There is a number of snuffs, sprays and gargles from which to choose. Some, by inflaming the mucosa, tend to prolong the condition they are intended to cure. Most troublesome to cure are chronic nasal carriers, who often have a double infection of *C. diphtheriæ* and *Str. hæmolyticus.* Boissard and Fry (1942) obtained favourable results from insufflations of sulphanilamide powder but, like other methods, this is not always successful. For some time penicillin lozenges (500 units) have been used in my wards for tonsillar carriers. The results have been good in a number of cases, but the time has not yet come to express a final opinion; penicillin, however, should certainly be tried, especially as supplies are now more readily available to the practitioner.

SCARLET FEVER.—It is anomalous that whereas the patient suffering from hæmolytic streptococcal tonsillitis plus a rash has to be notified as suffer-·ing from scarlet fever and isolated either at home or in hospital, another suffering from the equally infective condition of septic sore throat (minus the rash), caused by an identical strain of streptococcus, requires neither notification nor isolation, and after treatment for a few days with sulphonamides is allowed to return to school or work. Equally anomalous is it that scarlet fever patients are discharged from hospital without release cultures unless there is some obviously gross focus of infection, especially otitis media. Nevertheless, swabbing of the fauces, plating on blood agar, which may yield an almost pure culture showing the typical wide zones of hæmolysed medium around each colony, and the serological typing of the infecting strain, are of the utmost importance in institutional outbreaks of hæmolytic streptococcal infections, especially in maternity homes and nurseries. But the source of infection is not necessarily the fauces; it may be a whitlow on the finger of a nurse. By isolation and typing of the hæmolytic streptococcus it is possible to trace those who are infected with the same type and thus take steps to control the outbreak. Outbreaks due to a carrier, who may be found in the kitchen, are usually typified by "dropping" cases at irregular intervals. Carriers of the hæmolytic streptococcus respond, as a rule, to the

sulphonamides or to penicillin lozenges, although tonsillectomy may in some cases become necessary.

WHOOPING-COUGH.—In discussing the failure of isolation to control whooping-cough, it was said that one reason was the failure of parents to seek medical advice until too late to prevent the infection of contacts. Clearly, the ideal on both prophylactic and therapeutic grounds is to diagnose pertussis before the paroxysmal stage is established, but, even given the opportunity, this is not easy. It is therefore fortunate that laboratory aids to diagnosis are available. By the use of cough-plates or, preferably for infants and very young children who cannot cooperate, post-nasal swabs (Cruickshank, 1944), it may be possible to identify *H. pertussis* before the paroxysmal stage.

The post-nasal swab is easily made by bending the wire of an ordinary straight swab to a suitable angle so that it may be passed behind the uvula and rubbed firmly over the pharyngeal mucosa. Two precautions are necessary: experience shows that the swabbing should be carried out by the practitioner and not delegated to an attendant, and that the swab should be dispatched to the laboratory forthwith in order that a penicillin-treated plate of Bordet-Gengou medium may be inoculated as soon as possible.

H. pertussis is insensitive to penicillin—not so the concomitant flora which it inhibits, so providing a better field for the growth of *H. pertussis*. Failing the isolation of *H. pertussis*, valuable diagnostic aid is afforded by a differential white cell count; the conjunction of a suspicious cough with a count of 50,000 to 60,000 white cells, of which 70 to 80 per cent. are lymphocytes, is so highly suggestive as to justify isolation and observation.

IMMUNIZATION

The prophylactic measures so far discussed have, for the reasons stated, proved unsuccessful in the control of these common fevers. There remains to be considered the specific prophylactic measure of immunization which aims to raise the resistance, not to infection but to the results of infection with a specific causal agent. Artificial immunization may be active or passive; active immunization consists in provoking the tissues to produce antibodies by the injection of specific antigenic stimuli, e.g. diphtheria toxoid. Active immunity is slowly produced over a period of weeks and is durable. Although the level of antibodies falls with time, it is readily restored by an additional dose of the prophylactic. Passive immunity is quickly conferred by the injection of antisera but only endures for two to three weeks—the familiar prophylactic dose of diphtheria antitoxin at once comes to mind as an example. Sometimes the methods are combined; the child exposed to diphtheria may obtain immediate but temporary "cover" by passive immunization and this may be augmented and prolonged by a first injection of a toxoid prophylactic followed by at least one other dose at the appropriate interval, which differs with the prophylactic used. With this reminder of the differences between active and passive immunity, the available methods may be reviewed and assessed for each disease.

(1) *DIPHTHERIA.*—Mass active immunization of the child population in many American and Canadian cities has virtually eliminated, or greatly

reduced, the incidence of the disease. As the result of the intensive campaign instituted by the Ministry of Health in 1941, the annual incidence of, and deaths from, diphtheria have already been more than halved. Brincker (1945), in a valuable survey of results in England and Wales, shows that in 1937 there were, in round figures, 61,300 notifications (uncorrected for diagnosis) as compared with just under 30,000 notifications (corrected for diagnosis) in 1944. In 1937 the death rate per 100,000 children under fifteen years was 38.5 as compared with 9.2 in 1944. During 1945 over 600,000 children were immunized; notifications fell to 25,223 and deaths to 720—the lowest figures ever recorded. These figures speak for themselves; yet it is clear that much remains to be done; diphtheria is still a serious problem. Priority in immunization should, for obvious reasons, be given to children of pre-school age. The prophylactics used are alum-precipitated toxoid (A.P.T.), two injections, one of 0.2 c.cm. and the other of 0.5 c.cm., at an interval of not less than a month, and toxoid-antitoxin floccules (T.A.F.), three doses each of 1 c.cm., at intervals of two to three weeks; both are given intramuscularly. Current preparations of A.P.T. rarely give rise to serious reactions and may be used at any age, but if sensitivity is shown to the first dose of A.P.T. it is advisable, especially in adults, to change to T.A.F., which is unlikely to cause reactions at any age but is obviously less suited to clinic practice because of the additional attendance involved. There is a tendency to immunize in earlier infancy; eight months to one year is the age usually advised, but some would advocate, especially for the purpose of combining A.P.T. with pertussis vaccines (*vide infra*), an earlier start. Whatever the age of the infant at the time of the prophylactic course, it is advisable to give a re-inforcing dose at the time of school entry and subsequently at five-yearly intervals throughout school life.

(2) *WHOOPING-COUGH.*—Although it is common ground that the protection afforded by pertussis vaccines is not of the same order as that resulting from diphtheria prophylactics, the published results range from considerable success to virtual failure. There is no doubt that the discrepancies are, in part, due to the use of vaccines differently prepared, injected in different doses and at different intervals, and assessed, moreover, upon different criteria of immunity. Thus Sauer (1939), using a plain vaccine at weekly intervals in an aggregate dose of from 80,000 to 100,000 organisms, claimed a large measure of success in controlled field trials; Sauer *et al.* (1944), judging antigenic response by complement-fixation tests, found that a plain vaccine injected at three-weekly intervals, produced better results. Bell (1941) reported equally good results from two doses (interval four weeks) of an alum-precipitated vaccine. Sako *et al.* (1945), injecting an A.P. vaccine, 40,000 millions per c.cm., in three doses of 0.2, 0.3 and 0.5 c.cm., at four-weekly intervals in infants from two weeks to three months old, found that 78 per cent. had demonstrable antibodies four months after the last dose and 63 per cent. of 500 infants still had agglutinins two years later. Sauer *et al.* (1944) obtained the best results with a mixed diphtheria (A.P.T.) and pertussis vaccine given in three doses at intervals

of three or four weeks. Kendrick (1943) tried successively plain vaccines, A.P.-vaccines, and A.P.-vaccines combined with diphtheria toxoid. Compared with the controls, incidence was lower in each series and there was a greater proportion of mitigated attacks. Comparing only familial exposures, up to 36 per cent. of inoculated children and 92 per cent. of uninoculated children contracted pertussis; but it appears that the families in the inoculated series were on the average smaller than those in the uninoculated. On the other hand, McFarlan, Topley and Fisher (1945), using a plain vaccine in a long series of carefully controlled trials in Oxford, found no significant difference in incidence or severity between inoculated and control groups. Further observations are in progress. That, in brief, is the position. Although American workers report a considerable measure of success, it is, in my opinion, wiser to await developments before beginning vaccine prophylaxis on any large scale in this country. Once the most satisfactory type and dosage of vaccine are decided by rigorously controlled field trials upon a statistically significant scale, the subsidiary questions of combination with A.P.T. and the earliest age at which inoculation is likely to prove successful will be more easily settled.

(3) *MEASLES*.—Following the cultivation of the virus upon developing chick-embryo membranes and its attenuation through monkeys and human volunteers, Stokes and Rake (1940), Stokes *et al.* (1943), Maris *et al.* (1943), and Rake (1943), have succeeded in producing highly attenuated attacks of measles in children by intradermal injection, nasal instillation and, with more success, the inhalation of atomized sprays. If the results are confirmed on a large scale, it is clear that a long step forward has been taken in the control of measles.

Sero-prophylaxis in children exposed to measles has been practised for a number of years, using pooled convalescent or adult immune serum or parental whole blood, for one of two purposes: temporary prevention by passive immunization, or attenuation by injecting a smaller dose than that required for prevention or the same dose at a later stage of the incubation period. The following scale is suitable for children under three years of age; over that age the doses should be doubled (table 1).

TABLE 1

	Days after Exposure		
	1—5		6—9
	Prevention	Attenuation	Attenuation
Convalescent serum	5 c.cm.	2.5 c.cm.	5 c.cm.
Adult serum	10 c.cm.	5 c.cm.	10 c.cm.

Gamma globulin.—Current preparations will be superseded by gamma globulin, which is likely to be available in this country in the near future. Gamma globulin (Cohn *et al.*, 1944), is the most important of the three globulin fractions of blood serum and is believed to contain the antibodies to most of the common infections. It can be highly concentrated, and when buffered and stabilized may be heated for four hours at 57° C. This is important, because the virus of post-inoculation jaundice, transmitted

occasionally by human sera, is thereby destroyed. Greenberg *et al.* (1944), used G.G. in a fixed dose of 2 c.cm. for the protection of familial contacts. As controls, sixty-five children of similiar ages (six months to six years) were observed. The results were as follows:—

TABLE 2

	Protected	Modified measles	Unmodified measles
Gamma globulin	78 per cent.	21.3 per cent.	0 per cent.
Controls..			83 per cent.

G.G. prepared from the serum of convalescents has proved valuable in the control of outbreaks of infective hepatitis (Stokes and Neeve, 1945; Havens and Paul, 1945).

(4) *SCARLET FEVER.*—Active immunity to the erythrogenic toxin of the *Str. hæmolyticus* may be produced by a course of multiple skin-test doses of Dick toxin; it should be noted that the immunity conferred is anti-toxic only and its duration uncertain. Scarlet fever is now so mild, the requisite course of five injections so tedious and so liable to cause toxin reactions which may be more severe than a natural attack that, except in very special circumstances, the procedure is not worth while. Passive immunization with scarlet fever antitoxin is obsolescent and is giving way to prophylactic doses of sulphonamides or penicillin lozenges for the temporary protection of contacts.

References

Bell, J. A. (1941): *Publ. Hlth. Rep. Wash.*, **56**, 1535.
Boissard, J. M., and Fry, R. M. (1942): *Lancet*, i, 615.
Brincker, J. A. H. (1945): *Mon. Bull Min. Hlth.* and E.P.H.L.S., **4**, 214.
Cohn, E. J. *et al.* (1944): *J. clin. Invest.*, **23**, 417.
Cruickshank, R. (1940): *Lancet*, ii, 54.
—— (1943): *Brit. med. J.*, ii, 159.
—— (1944): *Lancet*, i, 176.
—— (1945): *Arch. Dis. Child.*, **20**, 145.
Gale, A. H. (1945): *Ibid.*, 1.
Greenberg, M., Frant, S., and Rutstein, D. D. (1944): *J. Amer. med. Ass.*, **126**, 944.
Halliday, J. L. (1928): *Med. Res. Coun. Spec. Rep. Ser.*, No. 120.
Havens, J., and Paul, J. R. (1945): *J. Amer. med. Ass.*, **129**, 220.
Kendrick, P. L. (1943): *Amer. J. Hyg.*, **38**, 193.
McFarlan, A. M., Topley, E., and Fisher, M. (1945): *Brit. med. J.*, ii, 205.
Maris, E. P., Rake, G., Stokes, J., Shaffer, M. F., and O'Neil, G. C. (1943): *J. Pediat.*, **22**, 17.
Rake, G. (1943): *Ibid.*, **23**, 376.
——, and Maris, E. P. (1943): *Ibid.*, **22**, 1.
Sako, W., Treuting, W. L., Witt, D. B., and Mickamin, S. J. (1945): *J. Amer. Med. Ass.*, **127**, 379.
Sauer, L. W. (1939): *Ibid.*, **117**, 79.
——, Ticker, W. H., and Markley, E. J. (1944): *Ibid.*, **125**, 949.
Stokes, J., O'Neill, G. C., Shaffer, M. F., Rake, G., and Maris, E. P. (1943): *J. Pediat.*, **22**, 1.
——, and Neeve, J. R. (1945): *J. Amer. med. Ass.*, **127**, 144.
——, and Rake, G. (1940): *Science*, **92**, suppl., p. 10.

THE TREATMENT OF THE INFECTIVE DISEASES

By F. L. KER, O.B.E., T.D., M.B., CH.B

Deputy Medical Superintendent, Little Bromwich Hospital for Infectious Diseases, Birmingham.

THE importance of fresh air, rest and nursing in the treatment of the infective diseases has in no way been overshadowed by the more recent therapeutic discoveries. The patient suffering from a fever should be nursed in a well-ventilated room, the windows of which should be kept open at all times. Even in the coldest weather it is quite possible to keep a patient warm with extra blankets and hot-water bottles, provided that the bed is not in a direct draught. Children who will not keep under the blankets can be given gloves and extra woollens if necessary. The fresh air thus obtained diminishes restlessness, assists in the promotion of sleep and encourages the appetite, and so increases the resistance of the patient.

During the pyrexial stage of the illness *complete rest* is essential. This should be obtained by keeping the patient flat on his back with only one thin pillow. There are few cases in which this position is uncomfortable for the patient. The rest should be complete, in that the patient is fed, and he should not be permitted to do anything for himself. This period is in most cases of short duration, and activity can be increased by giving extra pillows as soon as the temperature has settled. In the enteric group of fevers it may be necessary to maintain the flat position for several weeks and therefore special attention must be paid to the skin.

The importance of rest in the treatment of diphtheria cannot be over-stressed. The smallest effort may have the most serious consequences in some cases. On account of the possible development of late complications the rest is for a long period, the length being determined for the sake of convenience by the antitoxin dosage required for treatment (see p. 181). In the event of complications, the flat position must be maintained until these have disappeared. Mild cases (4,000 units) require to be kept recumbent for three weeks, after which an extra pillow can be given and the patient is allowed to feed himself lying on his side. Reading may also be permitted at this stage and children can play with light toys. A third pillow, allowing the patient to sit up, is given a week later and after a further seven or ten days he may be allowed out of bed for increasing periods daily. The moderate cases (8,000 to 16,000 units) should be kept flat for five to six weeks and the severe cases (16,000 units and over) for seven weeks before a second pillow is given.

NURSING

In an infectious diseases hospital patients may be nursed in "open" wards, in barrier wards or in single isolation units. It is, however, outside the scope of this article to give a detailed account of the different procedures. The prevention of cross-infection, not only with another disease, but also the spread of complications, is an ever present worry and can only be controlled if nursing is maintained at a high standard.

The *elimination of toxins* is important in all febrile illnesses. This should be stimulated by care of the skin, by promoting diuresis and by ensuring regular movements of the bowels. Frequent daily sponging with soap and water ensures that the skin is kept in good condition. Pyrexia is a beneficial reaction and only hyperpyrexial levels call for interference. In these cases cold or tepid sponging, repeated at short intervals if necessary, is usually sufficient. It is seldom necessary to use antipyretics.

The *free administration of fluids* is necessary to promote diuresis. In many cases it is not sufficient merely to tell the patient to drink as much as possible, but the nurse will have to force fluids continually, especially in children. The importance of fluids is increased in patients who are receiving treatment with the sulphonamide group of drugs.

Aperients.—In adults, calomel, 3 grains (0.2 gm.), is probably the best aperient to use to get a good initial movement of the bowels, whilst grey powder or castor oil is usually effective in children. In diphtheria, aperients should be avoided and reliance should be placed on enemas, which should be continued every other day during the period the patient is lying flat.

The parched dry tongue and the sordes on the lips and teeth which are associated with fever call for frequent *oral hygiene*. Mouth washes with any suitable mild disinfectant help to moisten the mouth and to relieve the patient of the bad taste from which he suffers. In severe cases the application of borax and glycerin is beneficial. Local applications to the tonsils are of little if any value except in the case of Vincent's angina, when a solution of mapharside applied with a throat swab helps to clear the infection.

DIET

The increase of metabolism found in all febrile conditions requires careful consideration of the diet. In the acute stage, loss of appetite and even a dislike for food, together with the necessity of resting the digestive system, make it necessary to supply a fluid diet. The toilet of the mouth before and after the feeds helps to make this more acceptable. Milk must form the basis of the diet, but for those who dislike milk, and to provide variety, milk modifications may be used. Flavouring with coffee or chocolate, malted milk, ovaltine, ice cream and junket are all satisfactory alternatives. Glucose should be added to all feeds. The feeds should be given at two-hourly intervals and should not be left at the patient's bedside for him to sip

when he feels inclined. To assuage thirst, water flavoured with fruit juice and sweetened with glucose should, however, be constantly at hand and a chart kept of the quantity supplied in order to ensure that adequate quantities are being taken. The necessity for encouragement when required has already been stressed. For those patients who are able to take them, beaten eggs and cereals may form an addition to the diet. A warm drink at night helps to induce sleep.

After forty-eight hours the diet in most cases can be built up by the inclusion of soft foods and rapidly increased to a normal diet. Vitamin B may have a therapeutic value in diphtheria. Additional vitamins are not called for unless there is an obvious deficiency.

In *scarlet fever* a low protein diet is recommended for fourteen days in order to lessen the risk of albuminuria and nephritis.

In *diphtheria*, as soon as the throat condition permits, the diet should be increased fairly rapidly, most patients tolerating well a light ordinary diet. Vomiting in diphtheria is usually a sign of cardiac involvement and should it appear an immediate return to a fluid diet is indicated and rectal feeding should be established if fluids are not tolerated. Feeding by means of a nasal tube will have to be adopted in cases of pharyngeal paralysis.

Opinion is still divided as regards the feeding of those suffering from *the enteric group of fevers*. Some authorities recommend a full diet but probably more favour the milk diet. Three ounces of milk with one ounce of water should be given every two hours throughout the febrile period. Half an egg may be beaten up with the milk for two feeds in the twenty-four hours, and if desirable a teaspoonful of brandy may be added. Plain or milk chocolate and jellies are also well received and easily digested and help to relieve the monotony.

In *gastro-enteritis* it is preferable to restrict oral intake to water for the first twenty-four hours, during which period an aperient should be given. In cases of dehydration, glucose saline will be required, either by the subcutaneous route or by intravenous drip transfusion. In cases in which fluids are not well tolerated and vomiting persists for a prolonged period, a gelatinous form of food, such as groats or sieved rice pudding, when available, sometimes stops the vomiting.

Theoretically, predigested protein should be useful in the dietary of gastro-enteritis. In practice the present products, however skilfully disguised, are unpleasant to take and as a result are not well tolerated. In addition, frequent estimation of the blood urea is necessary, as predigested proteins are liable to cause uræmia if not carefully controlled.

DRUGS

Medication with drugs plays only a minor part in the treatment of the infective diseases. Their use is confined to symptomatic treatment. Anti-

pyretics should be avoided if possible. *Hypnotics* are necessary in some cases and the cause of the insomnia should be considered. For patients with severe headache, aspirin or phenacetin may be sufficient. Dover's powder is very useful in the over-anxious patient. In acute restlessness and convulsions, the use of chloral and bromide is valuable, especially in infants and children. When there is delirium, sulphonal is beneficial, but it takes some hours to act and may have to be aided by a small dose of paraldehyde.

Cardiac stimulants are of doubtful value. Digitalis is useless and may be harmful to the diphtheritic heart. Strychnine, preferably given hypodermically, and caffeine sodium salicylate may help some patients, and are worthy of trial. Strychnine is helpful if a patient has multiple paralyses during the sixth week.

Antispasmodics.—In severe cases of whooping-cough, belladonna is the best antispasmodic to reduce the frequency and severity of the spasms. The best method is to begin with 3 minims (0.18 c.cm.) four-hourly and increase the dose by a minim a day until it reaches 10 to 15 minims (0.6 to 0.9 c.cm.) four-hourly and then decrease by a minim (0.06 c.cm.) a day.

A good sedative cough mixture for use in measles is:—

Tincture of ipecacuanha ..	180 minims (10.5 c.cm.)
Compound tincture of camphor	240 minims (14 c.cm.)
Syrup of tolu	1 ounce (28.4 c.cm.)
Chloroform water	6 ounces (170 c.cm.)

60 to 240 minims (3.5 c.cm. to 14 c.cm.) four-hourly according to age.

SERA

Antitoxin remains at present the specific treatment for *diphtheria*. Dosage has always been a subject of controversy between the advocates of massive doses and those who prefer the use of minimal amounts. A good basis in the estimation of the amount of antitoxin to be administered is to regard 8,000 units as the requisite dose for a throat which shows membrane covering both tonsils, unless these are grossly enlarged, when a further 8,000 units should be added. In mild cases with a small patch on each tonsil 4,000 units should be adequate, whilst in the case with a few specks and a positive swab, 2,000 units should be given. When the membrane has spread over the faucial pillar and on to the soft palate or into the nasopharynx, or both, increase in dosage is indicated and at least half of the total amount should be given intravenously. General toxicity and cervical adenitis' should likewise be considered in the estimation of the amount of antitoxin required. The most severe case should be adequately treated if given 80,000 to 100,000 units. If there is a further spread the intramuscular dose can be repeated within twenty-four hours. In diphtheria confined to the nose 4,000 to 8,000 units should be given, whilst laryngeal diphtheria is adequately treated with a dose of 4,000 units. Many cases of diphtheria have a concurrent streptococcal infection and routine administration of 3,000 units of antistreptococcal serum is advantageous.

Antistreptococcal serum should be given in cases of *scarlet fever*, *erysipelas* and *puerperal sepsis*. A dose of 3,000 units is adequate for the majority of cases. A severe case requires double the quantity. Intravenous administration of serum, repeated after twelve hours if necessary, should be the route of choice in the treatment of toxic and septic cases of scarlet fever. The modern refined sera produce a very small percentage of serum reactions. The usual precautions for serum sensitivity should be adopted in cases with a previous history of serum administration or in asthmatic subjects. Adrenaline should always be given if serum is administered intravenously.

CHEMOTHERAPY

THE SULPHONAMIDES.—The introduction of the sulphonamide group of drugs has completely altered the treatment of *cerebrospinal meningitis* and has been responsible for a remarkable fall in the mortality rate. Repeated lumbar puncture and serum therapy have become unnecessary, the former being required for diagnosis only. Treatment of meningitis requires maximal doses and as a result close supervision, so that only in exceptional cases should treatment be attempted at home. The risk of underdosage is to produce a chronic sulphonamide-resistant meningitis which, if not fatal, may result in hydrocephalus and optic atrophy.

The sulphonamides are also useful in the treatment of the secondary infections which cause broncho-pneumonia in *measles* and *whooping-cough*. Their use as a routine in the treatment of *scarlet fever* is disappointing but may help to clear otitis media should it complicate the case. It is recommended that sulphonamides should not be used until the ear is discharging. The administration of sulphonamides in addition to serum to patients with *erysipelas* brings rapid improvement, especially in the general condition.

Dosage.—There is a wide range of sulphonamides to choose from but for general use either sulphathiazole or sulphadiazine are the least toxic and the most effective. New members of the group are still being introduced, some of which require less frequent dosage to maintain the necessary blood level and may, after further trials, replace the present ones. In the use of sulphonamides it is desirable to reach a high level in the first twenty-four hours and for this reason the initial dose requires to be large. In severe infections it is recommended that in an adult the initial dose should be 2 gm., to be followed by 1½ gm. four-hourly for three to four days. The dosage can then be reduced, either by giving a smaller dose four-hourly or lengthening the interval between the doses to six hours. Eight days should be considered a sufficient length of time for a course of sulphonamide. The oral route should be used except in special circumstances, such as persistent vomiting and inability to swallow in unconsciousness, when intravenous administration is advocated.

Children tolerate sulphonamides well, and about one-half the adult dose can be given to children. In babies one-third of the adult dose is recommended.

Sulphaguanidine and succinyl sulphathiazole are worthy of trial in cases of *dysentery*, but the results as a whole are disappointing. The dosage with these two substances is higher than for the others. An adult should receive an initial dose of 4 gm., followed by 3 gm. four-hourly.

PENICILLIN

There is still much work to be done before the true value of penicillin in the treatment of the infective diseases can be assessed. The present method of three-hourly injections is unpleasant for the patient and research into solutions for slower absorption will, it is believed, make the injections less frequent. Penicillin administered by inhalation will probably become the method of choice in the lung complications associated with measles and whooping-cough.

Severe cases of streptococcal infection react well to penicillin, especially if used in conjunction with serum therapy. Claims for dramatic results in the treatment of diphtheria should be regarded with reserve until more extensive results are published. Theoretically, it is unlikely that penicillin will take a place in the treatment of diphtheria unless administered in the first few hours of the disease. It is possible that early administration might stop the spread but it cannot neutralize the toxin which has already passed into the circulation. Penicillin tablets in the local treatment of carriers is worthy of trial.

Dosage is still very varied, but the following quantities have proved useful and are given as a guide: in children under the age of two, 5,000 units three-hourly, in older children 10,000 units and in adults 20,000 units, when dealing with a moderate infection. In severe cases double or even treble the amount will be required for each dose. The average duration of treatment is ten days. When used in the treatment of meningitis a daily intrathecal dose to a maximum of 15,000 units should be given in addition to the intramuscular injections for the first two or three days.

PROGNOSIS IN THE INFECTIVE FEVERS

BY H. STANLEY BANKS, M.D., M.R.C.P., D.P.H.

Medical Superintendent, Park Hospital, London County Council.

THERE are four main factors affecting prognosis generally in the infective fevers: these are (1) the type of disease contracted; (2) specific immunization of the patient; (3) chemotherapy; (4) general resistance, as represented by the age and physical state of the patient. The order of relative importance of these factors was very different up to ten or twenty years ago, when general resistance occupied at least the second place. It is a measure of the degree of control of acute infections achieved by modern methods of immunization and treatment, that a factor of primary significance in fevers throughout the ages, i.e., the general resistance of the patient, should, except in extreme instances, be relegated to a place of minor importance in prognosis.

(1) *The type of disease contracted.*—As an epidemic gathers force, and especially when it is near to its peak, a much higher proportion of severe cases occur than in times of sporadic incidence. For example, in the war-time outbreak of cerebrospinal fever which reached high peaks of incidence about March in each of the years 1940, 1941 and 1942, a relatively large number of fulminating and encephalitic cases were seen in the winter and spring of those years. The increase in clinical severity in such cases may be explained by a step-up in virulence of the causal organism by rapid passage from case to case. As the epidemic wanes, the organism has to contend with an increase of communal immunity, since an ever increasing number of persons have experienced the infection without developing clinical disease. This brake on the progress of the organism reduces its virulence, with the consequent appearance again of milder cases except, here and there, when a particular individual is attacked who has failed to develop any immunity.

Again, for reasons ill-understood, a profound biological change may take place in the type of organism of a particular disease prevailing in a community at a given time. Hypertoxic or malignant diphtheria, for example, began to be much more prevalent in certain parts of Europe, especially Germany, from about 1927 onwards. In the Virchow Krankenhaus, Berlin, the diphtheria case fatality rate rose from 5 per cent. in 1924 to 26.7 per cent. in the first five months of 1927 (Deicher, 1927). Similarly in Leeds, the hospital case fatality rate for diphtheria rose from 4 to 14 per cent., due almost entirely to a great increase in hypertoxic cases (Anderson *et al.,* 1931). This was the time when the *gravis* type of diphtheria bacillus was differentiated from the other main types. It has since become clear that when the gravis or intermediate types first become established in strength in a community, these hypertoxic cases are apt to appear in considerable numbers. In London, this happened about 1934, and the rise which then

.occurred in hypertoxic cases coincided with a corresponding decrease in laryngeal cases and in the mitis type of bacillus. The same kind of change occurred in Scotland about 1940 (Carter, 1944). Scarlet fever, possibly for similar reasons, has shown four alternate waves of mildness and severity in the last two-and-a-half centuries: it has become gradually milder in Britain during the present century. This clinical change has not yet been correlated here with any known bacteriological change, but in Rumania, the severe type of scarlet fever with fatality rate of about 20 per cent., has been shown to be associated with the establishment in a district of the type 10 hæmolytic streptococcus (Schwentker *et al.*, 1943).

In the biennial epidemics of measles which appeared regularly in London and other large centres up to the outbreak of war, a change to a milder clinical type occurred in 1935-36. This change occurred before the application of sulphonamide therapy and was independent of any method of artificial immunization. In 1915, typhus fever devastated Serbia and, amongst many others, no less than two-thirds of the Serbian doctors lost their lives. During the recent war, when typhus fever was again prevalent in the Balkans, the majority of the cases were mild and mortality low. This was probably due to a rise in communal immunity, since the disease was endemic in certain parts, e.g., Bosnia, during the whole of the inter-war period.

(2) *Specific immunization.*—This is a most important factor in the prognosis of the individual case, particularly in diphtheria, smallpox, enteric and typhus fevers. The national campaign for diphtheria immunization was inaugurated in this country in 1940. Notifications and deaths began to fall significantly in 1942, when the number of immunized children reached 50 per cent.

At the end of 1943, about half the population could be assumed to have had immunizing injections. During 1943, the estimated rate of dying from diphtheria was 25 times as great among the non-immunized as among the immunized (Min. Hlth., 1944), and in 1944 it was 27 to 28 times as great. In fever hospitals the effect of immunization on gravis infections is seen almost daily. Often in such cases the disease is so mild as to be difficult to recognize clinically as diphtheria.

The paucity of cases of typhoid and paratyphoid fevers among troops inoculated with T.A.B. vaccine in two world wars, compared, for example, with those in the South African war, is well known. Antityphoid inoculation cannot, however, be relied upon to modify an attack if it occurs in the inoculated. Typhus vaccine was uniformly successful in the later stages of the recent war in preventing and modifying typhus fever among military and civil personnel exposed to gross infection.

(3) *Chemotherapy.*—Throughout the whole range of the specific fevers and their complications, the control of infections with hæmolytic streptococcus, staphylococcus, pneumococcus, meningococcus, gonococcus or

Bacterium coli by sulphonamides or penicillin, has vastly improved the prognosis.

(4) *General resistance—age and physical condition.*—Age is still a factor of primary importance in diphtheria and in whooping-cough of infants. It is less important than it was in cerebrospinal fever and most forms of pneumonia, thanks to chemotherapy. In typhus fever in the middle aged and elderly, previous immunization with typhus vaccine usually discounts the effect of age. Severe chronic intercurrent disease, e.g., chronic nephritis, diabetes, hypertension, chronic bronchitis, myocarditis, hepatic cirrhosis and all such degenerative diseases still have a serious effect upon prognosis, although not generally to the same extent as formerly.

SPECIAL FACTORS IN PROGNOSIS

Diphtheria.—Prognosis varies according to the age of the patient, the site, character and extent of the membrane, the length of time which has elapsed between onset and specific treatment, and the adequacy of the dosage and the route of the antitoxin. The younger the patient in hypertoxic and laryngeal diphtheria, the more serious the prognosis. In the former, the age-group three to six years, and in the latter that under eighteen months, are especially bad periods. When antitoxin is given on the first day, fatality is low, but it increases with each subsequent day. Large doses, e.g. 100,000 to 200,000 units intravenously, can save many lives in severe toxic diphtheria, especially in the older age-groups, that would be lost if smaller and intramuscular doses were given.

Thin, glistening, ill-defined membrane, rapidly spreading over the faucial pillars, uvula, soft palate and pharynx, accompanied by œdema (painless), is much more serious than thick, dull, well-defined membrane limited to the tonsils and without much œdema. Periglandular œdema ("bull-neck"), which will be present in the former case and not in the latter, is another serious sign. These are the two cardinal signs of hypertoxic diphtheria.

Petechial hæmorrhages, unless they first appear *after* adequate antitoxin has been given, practically always indicate a fatal degree of toxæmia. Heavy albuminuria is unfavourable, but anuria is almost always fatal. Pallor and cyanosis before specific treatment suggest early and dangerous circulatory failure; waxy pallor is even more ominous. Slow resolution of the membrane and of the periglandular œdema are unfavourable factors. The earlier the onset of circulatory failure, e.g., from the fifth to the twelfth day, the worse the prognosis. Cardiac vomiting at this period is a bad sign. There is a critical time about the sixteenth day. If the first appearance of cardiac weakness and vomiting is delayed until a few days before that time, there is usually hope, and if the patient survives the sixteenth day, recovery is usual. The prognosis in the respiratory and pharyngeal paralysis of the fifth to seventh week has been greatly improved by the use of breathing machines. The " iron lung " or Drinker apparatus has saved many lives in such cases.

These forms of paralysis are, however, largely prevented by the use of intravenous antitoxin in the acute stage of severe cases. In laryngeal diphtheria the danger is not from toxæmia but from asphyxia and bronchopneumonia. In the former, aspiration of the membrane through the direct laryngoscope saves many lives and avoids the operative mortality of tracheotomy. In the latter, penicillin has greatly improved the prognosis.

The ultimate prognosis of myocarditis and paralysis is good, at least in young subjects. In elderly subjects, however, there may be some residual myocarditis.

Scarlet fever.—Fatality rates in the simple type of scarlatina now prevailing in this country are as low as 0.1 to 0.5 per cent. In the rare form of toxic or malignant scarlet fever with peripheral circulatory failure and symptoms of shock, the prognosis is bad. A large dose of streptococcal antitoxin, e.g., 80,000 units, should be given intravenously as soon as possible. In the septic or anginose type of scarlet fever, antitoxin is also indicated intravenously and should be combined with sulphathiazole or penicillin. With such treatment prognosis is good. Complications occasionally cause sequelæ of a chronic nature, e.g., nephritis and carditis. These are rare in cases well treated with antitoxin. Chronic otorrhœa, with deafness and its cerebral accompaniments, is still by far the most frequent sequel of scarlatina. It should, however, now be entirely prevented. by prompt and adequate treatment of the acute otitis media with sulphathiazole or penicillin. In London, sulphathiazole-resistant strains of hæmolytic streptococcus now often crop up in the ear discharge. Therefore if there is lack of response to sulphathiazole after a few days, a switch should be made to penicillin without delay. These measures not only prevent chronic otorrhœa, but also many mastoid operations.

Measles.—Special factors in prognosis are the nutritional status and age of the child. Florid rickets, still often seen in northern districts, is apt to be associated with broncho-pneumonia and enteritis. Measles is generally mild up to the age of six or seven months. The period of highest fatality is between nine months and two years. After three years, fatality rapidly decreases and after five years is negligible in countries where measles is endemic.

In 1931-1932, out of 11,526 cases admitted to the London fever hospitals, the case fatality rate was 5.6 per cent. In 1942, out of 4,354 cases so admitted, it was only 0.38 per cent. This reduction to one-fifteenth of the former figure was only partially due to the milder type of disease but mainly due to the use of sulphonamides in broncho-pneumonia. In the Park Hospital every child under five years admitted with measles has, since 1940, received prophylactic sulphathiazole, 0.5 gm. six-hourly for about six days from the appearance of the rash. The apparent result is a considerable fall in the incidence of broncho-pneumonia and otitis media. Indeed, the three rarer complications, laryngitis, convulsions and enteritis, are now more formidable than broncho-pneumonia. Association of the acute stage of measles with

other infective diseases, e.g. laryngeal diphtheria or whooping-cough, is always serious. The former is rapidly fatal unless promptly recognized and treated with antitoxin.

Post-measles encephalitis is rare, about 1 in 2,000 cases, and the fatality rate is also low, about 10 per cent. In the remainder, recovery is complete without sequelæ. Septic ophthalmia, formerly a potent cause of corneal ulcer and partial blindness, is now, as a rule, rapidly cured by sulphathiazole or penicillin. Pulmonary fibrosis and bronchiectasis, which formerly so commonly followed the broncho-pneumonia of measles, should in future be rare when the acute condition is adequately treated. Hence the importance in remote prognosis of adequate chemotherapy for every child suffering from acute broncho-pneumonia.

Whooping-cough.—As in measles, the age and nutritional status of the child are important in prognosis. Infants under three months are prone to infection and have a high fatality due to asphyxia during a spasm, convulsions, broncho-pneumonia and pulmonary collapse. All new-born and very young infants should be specially shielded from contact with whooping-cough. Malnutrition or avitaminosis predispose to convulsions, hæmorrhage, bronchitis, pneumonia and enteritis, and greatly worsen the prognosis.

Chemotherapy has been disappointing in a considerable proportion of cases of broncho-pneumonia in whooping-cough. The infecting organism in such cases may be *H. Pfeiffer*, *H. pertussis*, a virus or other organism insensitive to sulphonamides or penicillin. An adverse factor in this broncho-pneumonia is the localized pulmonary collapse so often associated with it. When areas of pulmonary collapse are substantial, convulsions not infrequently complicate the condition. Very young infants, too, are more liable than others to catch the infection of non-specific gastro-enteritis. On account of these factors the mortality from whooping-cough has not fallen to the same degree as that from measles since the advent of chemotherapy. In the years 1933 to 1937, over 2,000 cases of whooping-cough per annum were admitted to the London fever hospitals, and about 8 per cent. died. For the two-year period 1939-40, in a similar number of cases, the fatality rate was 3 per cent.—a substantial reduction but by no means a negligible mortality. For the same reasons, residual pulmonary fibrosis after whooping-cough is still an important factor in remote prognosis. Rare nervous sequelæ, possibly due to cerebral hæmorrhage, are hemiplegia, upper neurone paralysis, aphasia, blindness and deafness. Certain psychopathic sequelæ in "problem" children have been suggested (Lurie and Levy, 1942), but no real proof has been adduced in support of the idea.

In children who have been inoculated with phase I *H. pertussis* vaccines and who contract whooping-cough, there is some evidence that the attack may be modified. Recently, however, the value of prophylactic immunization in this disease has been subjected to damaging criticism (McFarlan *et al.*, 1945; Doull *et al.*, 1939). In these well-conducted controlled experiments

no significant difference could be demonstrated as regards attack rate between the groups of inoculated and of uninoculated children.

Cerebrospinal fever.—The prognosis has been immensely improved by treatment with sulphathiazole or sulphadiazine. In military hospitals, both U.S. and British, many large series of cases have been recorded with a fatality rate for young soldiers of only 1 or 2 per cent. Among 500 cases of all ages treated at the Park Hospital from 1939 to 1943, the fatality rate was only 6 per cent. The worst age-groups are under twelve months and over fifty years. Fulminating cases with massive purpura and adrenal hæmorrhage are usually too rapidly fatal for chemotherapy to be effective, but there are a few exceptions. Encephalitic cases with persistent deep coma, formerly called the "acute fatal type", nearly always die, but again a few recoveries are reported. There are still also some puzzling autopsies seen in this disease, in which the meningitis is resolving and the precise cause of death cannot be ascertained. There is no adequate evidence so far that penicillin gives better results than sulphathiazole.

Enteric fever.—Except for broncho-pneumonia, the prognosis in the principal complications—toxæmia, perforation and hæmorrhage—has not been greatly improved by modern treatment. There is some evidence that hæmorrhage may be associated with low platelet counts and that it may be prevented or ameliorated by large doses of vitamin C, e.g. 1,200 mgm. daily (Drummond, 1943). In an attempt to combat the toxæmia in severe cases the Felix antityphoid serum has been used during the last ten to twelve years. Results have been inconstant, but not usually good. If the diagnosis could be made by blood culture in the first week of the disease and the serum given then, results might be better.

Although antityphoid inoculation brilliantly protects against attack, when an inoculated person contracts the disease the prognosis may not be better than in the uninoculated. The case fatality rate of typhoid fever throughout the British Army in the first four years of the late war was 17 per cent. In a series of eighty well-inoculated soldiers in the Middle East, most cases were severe and the fatality rate was 11 per cent. (Jordan and Everley Jones, 1945). On the other hand, there is some recent evidence from the U.S. Army in the Far East that the attack in the inoculated may be modified.

Smallpox.—Prognosis in variola major depends chiefly upon (1) the vaccinal condition and (2) whether the eruption is hæmorrhagic, confluent or discrete. Recent vaccination not only prevents but greatly modifies an attack. Purpuric smallpox indicates overwhelming toxæmia and is invariably fatal. When hæmorrhage is confined to the pocks, prognosis depends more upon confluence of the eruption than upon hæmorrhage. Confluent smallpox has a fatality of 40 to 50 per cent., unless there is sufficient residual vaccinal immunity to modify the maturation of the lesions. In the latter case, the pocks may dry off quickly and life be saved. There is recent evidence that penicillin will greatly improve the prognosis in confluent smallpox by

overcoming the staphylococcal infection of the pustular stage. (Jeans *et al.*, 1944.) In discrete variola major the fatality is 6 to 8 per cent. In variola minor, fatality is negligible and complications few. Among 13,686 cases of variola minor treated in a London hospital from 1928 to 1934, the case fatality rate was only 0.25 per cent. (Marsden, 1936).

Chickenpox.—Prognosis is good except for very rare types or complications. The severe toxic form, varicella hæmorrhagica, is exceedingly rare but is generally fatal. Varicella bullosa is due to secondary infection with *Staphylococcus aureus*, and varicella gangrenosa generally to secondary infection with the hæmolytic streptococcus. Both these forms should now be promptly cured by sulphathiazole or penicillin. Encephalitis is a very rare complication, of which the fatality rate is as low as 6 to 10 per cent. (Waring *et al.*, 1942).

Rubella.—A word in conclusion about the prognosis of German measles in pregnant women. An Australian ophthalmologist first observed the association of congenital cataract and congenital heart lesions in infants with a history of rubella in the mother during the first two months of pregnancy (Gregg, 1941). Many subsequent observations have shown that rubella contracted during the first six weeks of pregnancy may produce generalized foetal infection with subsequent lesions of the eyes, both labyrinths and heart. When infection occurs between the sixth week and the end of the third month, the eyes, heart and semi-circular canals may be spared, but the cochlea may suffer, with consequent deaf-mutism; after the third month the probability of congenital malformations in the offspring becomes remote (Carruthers, 1945). The prognosis for the unborn child therefore depends upon protection of a non-immune mother from this infection during the first three months of pregnancy. If exposure occurs, an effort should be made to obtain some protection for the mother by injection during the early incubation period of convalescent or adult serum, placental extract or gamma globulin, if obtainable.

References

Anderson, J. S. *et al.* (1931): *J. Path. Bact.*, 34, 667.
Carruthers, D. G. (1945): *Med. J. Austral.*, 32, 315.
Carter, H. S. (1944): *J. Hyg.*, 43, 341.
Deicher, H. (1927): *Deutsch. med. Wschr.*, 53, 1555.
Doull, J. A., *et al.* (1939): *Amer. J. Dis. Child.*, 58, 691.
Drummond, J. (1943): *Clin. Proc.*, 2, 65.
Gregg, N. M. (1941): *Trans. Ophthalmol. Soc. Austral.*, 3, 35.
Jeans, W. D., Jeffrey, J. S., and Gunders, K. (1944): *Lancet*, ii, 44.
Jordan, J., and Everley Jones, H. (1945): *Ibid.*, ii, 333.
Lurie, L. A., and Levy, S. (1942): *J. Amer. med. Ass.*, 120, 890.
McFarlan, A. M., Topley, E., and Fisher, M. (1945): *Brit. med. J.*, ii, 205.
Marsden, J. P. (1936): *Spec. Rep. L.C.C.*
Ministry of Health (1944): *Bull. E.P.H.L.S.*, 3, 142.
Schwentker, F. F., *et al.* (1943): *Amer. J. Hy.*, 38, 27.
Waring, J. J., *et al.* (1942): *Arch. int. Med.*, 69, 384.

SMALLPOX IN THE VACCINATED

By E. T. CONYBEARE, M.D., F.R.C.P.,

Medical Officer, Ministry of Health.

For more than ten years, outbreaks of smallpox occurring in this country have been local in character and limited in extent. The disease has not been endemic but connected either with recognized cases arriving from abroad or with the handling of infected merchandise, such as raw cotton. During the first six months of 1946, over 50 cases were notified in England and Wales and the total for the year seems likely to be greater than that for any year since 1934. About this time many troopships, carrying patients who had sickened during the voyage, arrived at English ports from Bombay, where smallpox was prevalent. It was not possible to quarantine the numerous contacts of these ship-borne cases and the main barrier against spread of infection to the home population was vaccination or re-vaccination before disembarkation plus follow-up and surveillance by the staffs of local authority health departments. Recently, smallpox has also been brought into this country by air travellers from the Far East. Introduction by this means is particularly difficult to control because the short duration of the air journey permits the arrival of persons not known to be contacts but who may nevertheless already be infected and within the incubation period of the disease. All air travellers landing in this country are now given special cards warning them of the possibility of developing smallpox after arrival. Also by this means they are urged to seek medical advice promptly should they become ill, however slightly, and to inform the practitioner they consult of their recent journey. Although the immediate danger from ship-borne smallpox is likely to decrease, that from air-borne infection will probably become increasingly serious. It is indeed unlikely that this country can continue to enjoy the relative freedom from smallpox which was so marked a feature of the years immediately before and after the outbreak of war in 1939.

In several recent outbreaks caused by smallpox contacts arriving in this country from abroad, attention has been drawn to the occurrence of the disease in vaccinated persons, among whom it sometimes produces forms of clinical illness which are difficult to recognize as smallpox and which escape detection as such until there has been spread of the infection to persons who show a florid form of the disease. Propagandists against vaccination have exaggerated this phenomenon, but there is, as has been pointed out by Stevenson (1944), nothing new in such occurrences. The standard textbooks of medical practice when dealing with smallpox describe mainly the more readily distinguishable forms of the disease likely to be seen in unvaccinated persons, or in those whose immunity artificially conferred by vaccination has declined. It is only in works of a more specialized kind,

overcoming the staphylococcal infection of the pustular stage. (Jeans *et al.*, 1944.) In discrete variola major the fatality is 6 to 8 per cent. In variola minor, fatality is negligible and complications few. Among 13,686 cases of variola minor treated in a London hospital from 1928 to 1934, the case fatality rate was only 0.25 per cent. (Marsden, 1936).

Chickenpox.—Prognosis is good except for very rare types or complications. The severe toxic form, varicella hæmorrhagica, is exceedingly rare but is generally fatal. Varicella bullosa is due to secondary infection with *Staphylococcus aureus,* and varicella gangrenosa generally to secondary infection with the hæmolytic streptococcus. Both these forms should now be promptly cured by sulphathiazole or penicillin. Encephalitis is a very rare complication, of which the fatality rate is as low as 6 to 10 per cent. (Waring *et al.*, 1942).

Rubella.—A word in conclusion about the prognosis of German measles in pregnant women. An Australian ophthalmologist first observed the association of congenital cataract and congenital heart lesions in infants with a history of rubella in the mother during the first two months of pregnancy (Gregg, 1941). Many subsequent observations have shown that rubella contracted during the first six weeks of pregnancy may produce generalized foetal infection with subsequent lesions of the eyes, both labyrinths and heart. When infection occurs between the sixth week and the end of the third month, the eyes, heart and semi-circular canals may be spared, but the cochlea may suffer, with consequent deaf-mutism; after the third month the probability of congenital malformations in the offspring becomes remote (Carruthers, 1945). The prognosis for the unborn child therefore depends upon protection of a non-immune mother from this infection during the first three months of pregnancy. If exposure occurs, an effort should be made to obtain some protection for the mother by injection during the early incubation period of convalescent or adult serum, placental extract or gamma globulin, if obtainable.

References

Anderson, J. S. *et al.* (1931): *J. Path. Bact.,* **34**, 667.
Carruthers, D. G. (1945): *Med. J. Austral.,* **32**, 315.
Carter, H. S. (1944): *J. Hyg.,* **43**, 341.
Deicher, H. (1927): *Deutsch. med. Wschr.,* **53**, 1555.
Doull, J. A., *et al.* (1939): *Amer. J. Dis. Child.,* **58**, 691.
Drummond, J. (1943): *Clin. Proc.,* **2**, 65.
Gregg, N. M. (1941): *Trans. Ophthalmol. Soc. Austral.,* **3**, 35.
Jeans, W. D., Jeffrey, J. S., and Gunders, K. (1944): *Lancet,* ii, 44.
Jordan, J., and Everley Jones, H. (1945): *Ibid.,* ii, 333.
Lurie, L. A., and Levy, S. (1942): *J. Amer. med. Ass.,* **120**, 890.
McFarlan, A. M., Topley, E., and Fisher, M. (1945): *Brit. med. J.,* ii, 205.
Marsden, J. P. (1936): *Spec. Rep. L.C.C.*
Ministry of Health (1944): *Bull. E.P.H.L.S.,* **3**, 142.
Schwentker, F. F., *et al.* (1943): *Amer. J. Hy.,* **38**, 27.
Waring, J. J., *et al.* (1942): *Arch. int. Med.,* **69**, 384.

tion failed to take or that any immunity which it did produce has sub-sequently fallen to a negligible level. A response to re-vaccination, which is commonly described as an "accelerated take" or vaccinoid reaction, probably indicates an immunity which was definitely on the wane but which the re-vaccination will promptly boost to a high level. When, however, re-vaccination either fails to produce any skin reaction at the site of insertion, or at the most results in an immediate but transient wheal and erythema, the position as regards protection against smallpox is uncertain. Some authorities are content to accept such a response, if repeatedly obtained, as an indication of complete immunity, whereas others maintain that this assumption is unwarranted. It is certainly my experience that doctors and nurses exposed to smallpox and presumably immune usually show when re-vaccinated a skin reaction which consists of the development of an "itchy papule" at the site of insertion on about the third day, but which by the sixth day has subsided without the formation of a vesicle.

CLINICAL ASPECTS

The immunity induced by vaccination being a complicated process it is not surprising that the clinical appearances of smallpox in vaccinated persons are extremely variable and that they range from a mild illness resembling influenza and without any focal eruption (the so-called *variola sine eruptione*) through forms with a more or less characteristic eruption to severe illnesses fatal from toxæmia before the focal eruption appears. The milder and also the more severe forms abound in problems of clinical diagnosis. Smallpox of any kind, even the form without a focal eruption, always provides an urgent administrative problem for the local health officer.

The useful but arbitrary clinical classification of smallpox cases into six groups of graduated severity introduced by Ricketts in 1893 and later used by Marsden (1936) does not appear readily applicable to smallpox in vaccinated persons, and for this purpose it is believed that a division into four clinical categories will be more useful.

(1) *CASES WITHOUT FOCAL ERUPTION.*—It has been mentioned above that when vaccinal immunity begins to wane, protection against the toxæmic fever sometimes seems to be lost or diminished before susceptibility to any form of focal eruption returns. Vaccinated persons infected at this early stage of waning immunity may react with a brief feverish illness, which can be confirmed by serological tests as a form of smallpox. This illness has frequently been described under such names as "*variola sine eruptione*" and "contact fever". It is probably more common in vaccinated smallpox contacts than is generally realized. The moderate fever of sudden onset lasts for only two or three days and there are no localizing signs. At the bedside, differentiation from virus influenza is difficult, except possibly by the unusual severity of the associated headache. Transient miliarial or morbilliform rashes sometimes occur as they do during the

such as the now almost classical treatise of Ricketts and Byles (1908) and the more recent monograph by Marsden (1936), that there can be found a full description of the modified but not less important forms of variola. In this article it is hoped, mainly by an account of recent experience, to stimulate reference to these authoritative works rather than to abstract or condense them in respect of a particular and perhaps somewhat neglected aspect of smallpox.

VACCINATION AND SMALLPOX IMMUNITY

The smallpox immunity likely to result from the vaccination of a particular individual may be influenced by many variables, among which the most important are probably the capacity of the individual to react to an artificial infection, the potency of the strain of vaccinia used, and the technique of lymph insertion. The protective effect of vaccination is most evident in relation to the focal eruption of smallpox, which can be profoundly affected in two ways. In the first place, the numerical severity of the rash can be reduced by all degrees from the maximum of confluence on maturity over the greater part of the body down to complete extinction. Secondly, the whole or part of the lesions can be considerably modified in respect of size, position in the skin, speed of development and the stage at which resolution and healing occurs. Vaccination can also shorten in duration, reduce in severity or abolish altogether the so-called pre-eruptive or toxæmic fever.

It is interesting and clinically important that of the three main effects of vaccination the first to develop is the reduction in the numerical severity of the eruption, the next being the effect on the course and character of the individual lesions and the last the immunity to the toxæmic fever. When a complete immunity to smallpox conferred by vaccination wanes, it appears that there is first a return of liability to the toxæmic fever, then a return of susceptibility to eruptions of varying numerical severity, but in which a majority of the lesions are still very much modified and, finally, a complete loss of all artificial immunity so that there is liability to rashes of maximum numerical and lesional severity, and even susceptibility to toxic forms of the disease which prove fatal before the outcrop of a focal eruption.

Assessment of immunity.—A precise assessment of the degree of immunity possessed by a vaccinated person is at present impossible. There is nothing in this field comparable to the Schick test in diphtheria. It is true that antibody to the variola and vaccinia viruses can be detected in the serum of vaccinated persons (Downie, 1946), but the correlation of these laboratory findings with clinical observations of immunity has not yet been defined with sufficient precision for them to be useful as a check on the result of vaccination. It is probable, however, that some indication of individual capacity to resist smallpox may be obtained by a careful observation of the skin reaction at the site of a re-vaccination. When this resembles a successful primary vaccination it seems reasonable to assume either that the previous vaccina-

composing the eruption the less evident are the important distributive features upon which a confident clinical diagnosis so much depends. With a minimal eruption the lesions lack the uniformity of character and development which is a useful guide in cases with a more pronounced eruption. Mild chickenpox, acne and, in children, lichen urticatus, seem to be the most frequent misdiagnoses in such cases. The paucity of the eruption is sometimes a useful point against a diagnosis of varicella, especially when the pre-eruptive fever has been severe and of several days' duration, as it often is, even when the subsequent focal eruption is mild. As being against a diagnosis of acne there may be noted the rapidity with which the eruption has developed, often in a matter of only a few hours, and the presence of pus-capped pimples on the wrists and backs of the hands. Absence of lesions on the face and the presence of irritation sufficient to induce scratching may help to exclude smallpox, especially in children. Rapid resolution of the lesions and crusting without pustule formation are not, however, against a diagnosis of smallpox in such cases.

In recently vaccinated persons showing a marked "primary intake" reaction at the site of insertion from the sixth to the tenth day there is a risk of diagnosing coincident mild smallpox as generalized vaccinia. Here, again, severity of the pre-eruptive constitutional disturbance may be the most useful clinical pointer to smallpox.

Laboratory tests.—Confident clinical diagnosis of cases of smallpox with a minimal focal eruption being often difficult and sometimes impossible, especially when the focal eruption is in its early stages, the wisest course may be to resort to a period of isolation and observation during which the development of the rash can be watched and help may be obtained from laboratory tests with cutaneous material derived from suitable lesions. The application of such tests has recently been described in some detail (Downie, 1946). Virus can sometimes be detected by the direct examination of stained smears from early lesions and a positive diagnosis of smallpox made rapidly in the course of a few hours. Variola antigen can be detected by a complement fixation test on vesicle fluid or crusts and, although it may take up to forty-eight hours or longer to obtain a result, this is probably the most valuable laboratory test at present available for the diagnosis of smallpox. Such tests considerably assisted clinical diagnosis in the following two cases:—

N.H., aged ten years, vaccinated in infancy, was a contact at home with her father who had a very mild attack of smallpox with a rash comprising only four lesions, and which was diagnosed in retrospect. After a feverish illness of three days' duration she developed an eruption comprising not more than twenty lesions but which involved the face, the upper part of the back and one thigh. Only one lesion was at all suggestive of a smallpox pustule and for the most part the eruption aborted at the papular stage without crusting. Stained smears of material from the more developed lesions were found by Professor A. W. Downie to show elementary bodies and he also obtained a positive complement fixation test to a titre of 1/1500 with vesicular fluid.

pre-eruptive fever of other forms of smallpox. In some of these cases, when the fever has lasted longer than three days, an X-ray picture of the lungs has shown appearances resembling those seen in so-called atypical pneumonia (Arnott and Howat, 1944).

As might be expected, most of the recorded cases of this type of smallpox illness have been nurses or doctors working with smallpox cases. In one outbreak (Conybeare, 1939) it is recorded that six out of sixteen such contacts of a fatal case of confluent smallpox experienced an illness of this type. The following is a more recent example:—

Nurse L. was primarily vaccinated at the age of twenty-two with the production of two foveated scars. Four years later and without further vaccination she began work in a smallpox hospital. Twelve days afterwards she developed fever, malaise and headache without localizing signs. The next day, still feverish, she presented a patchy morbilliform eruption on the chest and arms. On the third day of illness this rash entirely disappeared and the fever subsided. From this time she remained perfectly well and did not develop any other form of skin eruption. A specimen of blood taken on the tenth day after the onset of her illness was examined by Professor A. W. Downie and showed deviation of complement with variola-vaccinia antigen to a titre of 1/80.

The epidemiological importance of cases without focal eruption is uncertain. It has been stated (Ricketts and Byles, 1908) that the toxæmic or pre-eruptive fever of smallpox is not infective and therefore that danger need not be apprehended from cases without focal eruption. Up to date there is no published evidence against this view. Apart from the discomfort to the individual concerned, an illness of this type occurring in a doctor, a nurse or a sanitary inspector during the course of an outbreak of smallpox can cause considerable administrative inconvenience. It is evident that in order to avoid it all persons likely to have to deal with smallpox cases should be re-vaccinated as a routine at not less than yearly intervals. Re-vaccination just before or soon after exposure to infection does not always protect against this type of smallpox illness.

(2) *CASES WITH MINIMAL FOCAL ERUPTION.*—The total number of lesions composing the focal eruption of an attack of smallpox in a person with a high degree of vaccinal immunity may be very small and in such cases most, if not all, of the individual lesions tend to be very much modified. Eruptions undoubtedly caused by smallpox but comprising no more than three or four lesions are most often seen in those whose occupation obliges them to be re-vaccinated at frequent intervals. They sometimes occur in persons vaccinated several years previously when a precautionary re-vaccination has been performed either just before or just after a known exposure to infection. Eruptions of a slightly greater degree of numerical severity but comprising not more than a hundred or so lesions are not uncommon in children over the age of five years and others successfully vaccinated in infancy but whose immunity is on the wane.

These types of case present by far the most difficult diagnostic problems encountered in dealing with smallpox. The smaller the number of lesions

always show a centrifugal distribution pattern with the oldest lesions on the face and upper back. It has been observed, however, that the extensor limb surfaces are not always more heavily invaded than the flexor and that the axillæ are not always spared.

Diagnostic difficulty arises chiefly when the typical rash distribution of smallpox is imitated by the rash of another disease. Thus the characteristic centripetal distribution of the rash in varicella may sometimes be converted to an apparently centrifugal pattern by secondary factors, such as sunburn. Indeed this may account for the greater difficulty which often seems to be encountered in the differential diagnosis of variola and varicella in hot climates. The direct examination of smears from early lesions for the presence of elementary bodies was recently found to be of great help in dealing with coincident outbreaks of variola and varicella in a vaccinated community in the Middle East (Illingworth and Oliver, 1944). Diagnosis is also difficult in allergic and septic conditions of the skin which may produce rashes composed of a number of fairly close imitations of the typical smallpox lesion. In many such cases the absence of a characteristic pre-eruptive fever and an atypical distribution, for instance one in which the face may escape altogether, often enable smallpox to be excluded with confidence.

Vaccination within the incubation period, especially if it is done within three or four days of exposure to infection and there is a successful "primary take" reaction by about the sixth day, is sometimes followed by an attack of smallpox in which the focal eruption is numerically moderate. In my experience the individual lesions in such cases, although superficial, are large and not highly modified, except that they tend to resolve without much residual scarring. Distribution is typical of smallpox but there may be a concentration of lesions around the site of the vaccination. The pre-eruptive illness is usually quite severe but the subsequent constitutional disturbance negligible. Even when there is little or no pre-eruptive fever it would appear unwise to regard any such case as "generalized vaccinia", and in consequence to neglect strict isolation.

Of *laboratory tests* it may be said that whenever possible they should always be employed in cases of the moderate category of severity as regards focal eruption. Although decision as to immediate administrative measures will usually have to rest on the initial clinical impression, subsequent confirmation or otherwise from the laboratory serves as a useful check on the clinical findings. The weight to be attached to a negative clinical report on a case in which the clinical impression has been positive is a matter of careful judgement, taking into account all the circumstances. A positive laboratory report in the face of a negative clinical impression must of course be taken as conclusive.

Infective skin debris.—Cases with a moderate focal eruption shed considerable amounts of highly infective crust material containing living virus.

Mrs. C., aged sixty-seven, vaccinated in infancy and once re-vaccinated at the age of eighteen, nursed her married daughter who suffered an attack of smallpox with a numerically reduced and modified rash unrecognized except in retrospect. After three days of feverish illness with headache and vomiting, Mrs. C. developed an eruption comprising only thirteen lesions. The face, both wrists, the upper part of the back and one thigh were the sites of the eruption. Within forty-eight hours all except one lesion were small pustular pimples which within another week had resolved without scarring. One lesion, although small, was at forty-eight hours a circular vesicle resembling the characteristic variola lesion but very superficially situated. This crusted and scabs were examined by Professor A. W. Downie, who reported a complement fixation test with variola-vaccinia antigen up to a dilution of 1/1600.

The laboratory may also be of assistance when the diagnosis lies between smallpox and generalized vaccinia, but the inoculation and growth in the hen's egg necessary to distinguish the two viruses may take the better part of a week, and in such cases it may be preferable to act on a presumed but mistaken diagnosis of smallpox rather than to await a report which in any event may be inconclusive.

It is quite certain that cases with minimal numbers of highly modified lesions frequently spread infection and that the smallpox which they transmit, should it attack a person unprotected in some degree by vaccination, may not be modified but extremely severe. The sudden occurrence of severe smallpox in a susceptible person apparently unconnected with any known source of infection can often be attributed to a chain of mild cases with minimal rash, all of whom have escaped detection and gone about their work and social activities without restriction by illness. When an incident of this kind is suspected, cutaneous scarring usually helps but little in tracing the course of events but serological tests on blood specimens can be of much help, especially when there has not been a recent re-vaccination of the suspects.

Surveillance of known smallpox contacts should include a close watch for these mild forms of smallpox illness in which it is easy to miss the presence of a sparse focal eruption unless the whole of the body surface is inspected at frequent intervals, particular attention being paid to the face and wrists.

(3) *CASES WITH MODERATE FOCAL ERUPTION.*—A vaccinated person whose immunity has fallen well below the level giving complete protection may experience an attack of smallpox in which the number of lesions composing the focal eruption goes well beyond the arbitrary figure of 100 which can be taken as a rough limit for inclusion in the category of minimal focal eruption. In moderate category cases the rash may even approach confluence in certain areas without more than a few of the individual lesions exhibiting the development and appearance typical of variola. In general, however, the larger the number of lesions, whether modified or not, the more evident the characteristic features of distribution which are the best clinical basis for a positive diagnosis. In my experience cases of smallpox with an eruption of this order of numerical intensity nearly

eruption; but severe cases, and especially the toxic hæmorrhagic patients, seem to be infective before the outcrop of a focal eruption. It is possible that they disseminate virus in some manner other than from the skin, e.g., from the respiratory tract. There is no need to stress that all possible precautions are needed in dealing with such cases from the beginning of their illness.

SUMMARY

For this country at present, smallpox in the vaccinated seems to be of greater epidemiological importance than smallpox in the unvaccinated. This position is likely to continue until some better means of checking the result of a re-vaccination than casual observation of the skin reaction at the site of insertion becomes available. The clinical appearances of smallpox in the vaccinated are very variable and range from mild forms with little or no focal eruption to a severe illness which can be fatal before the focal eruption has time to appear. A classification based on clinical appearances is put forward in the belief that it may be useful in practice. Some of the many problems which occur in connexion with the diagnosis of smallpox in the vaccinated are discussed, and it is suggested that in future greater use should be made of laboratory tests on cutaneous material from suspected cases with a mild or moderate focal eruption. In dealing with a disease like . smallpox, in which the consequences for the community may be serious, none can be blamed for an over-cautious attitude which can·be extremely inconvenient for the individual patient. The help which can be given by the laboratory in the diagnosis of the difficult case is considerable and when available should not be neglected. It ought not, however, to form the only basis on which administrative and other decisions can be made with confidence.

References

Arnott, W. M., and Howat, H. T. (1944): *Lancet*, ii, 312.
Conybeare, E. T. (1939): *Ibid.*, i, 813.
Downie, A. W. (1946): *Mon. Bull. Min. Hlth. Emerg. Pub. Hlth. Lab. Serv.*, 5, 114.
Illingworth, R. S., and Oliver, W. H. (1944): *Lancet*, ii, 681.
Marsden, J. P. (1936): "A Critical Review of the Clinical Features of 13,686 Cases of Smallpox (Variola Minor)", London County Council, London.
Ricketts, T. F., and Byles, J. B. (1908): "The Diagnosis of Smallpox", London.
Stevenson, W. D. H. (1944): *Lancet*, ii, 697.

Full precautionary measures are needed in dealing with them, including particular care of laundry and bed linen. In the treatment of cases in this category and also of those in the mild category it may be possible, by the application of occlusive and virucidal paints, to limit the amount of potentially infective·skin debris which would otherwise have to be dealt with by disinfection of wards, bedding and so on. The constitutional condition of such patients is usually so good that it permits an intensive use of such treatment.

(4) *SEVERE CASES.*—In this category are those cases in which the focal eruption reaches the maximum numerical severity of confluence, at least on the face, with uniform typical lesions pursuing an unmodified course involving considerable suppuration. In such cases death is not uncommon following severe visceral hæmorrhage or secondary to septic absorption from the rash at a comparatively late stage of the illness. Also to be included are the cases in which the initial illness is exceptionally severe and accompanied by a generalized hæmorrhagic erythema. Such cases are often fatal before the outcrop of any focal eruption.

Although such severe forms of smallpox are practically unknown among persons whom it is reasonable to believe have been effectively vaccinated less than ten years before infection, it is a great mistake to suppose that a single successful vaccination producing a foveated scar or scars will confer a subsequent lifelong protection against smallpox in its severe forms. The following recent case is instructive in this respect:—

N.R., aged thirty-three years, had been vaccinated successfully with scar forma-tion in infancy but was not re-vaccinated before, during his work as a sanitary inspector, he dealt with the bedding of a vaccinated boy who had suffered an attack of smallpox in which the focal eruption was of a moderate order. Nine days later this man developed a high fever with severe headache and considerable prostration. On the third day of illness he had a generalized erythema with œdema of the skin, conjunctival hæmorrhages and numerous purpuric spots over the "bathing drawers" area. His liver became easily palpable and he died on the fifth day of his illness before any focal eruption had appeared. This patient probably infected his wife with smallpox before he was removed to hospital on the fourth day of illness.

The diagnosis of severe cases of smallpox with an extensive focal eruption approaching confluence can nearly always be made promptly without the assistance of laboratory tests, but toxic cases with a hæmorrhagic rash during the first few days of illness not uncommonly go unrecognized and are often admitted to general hospitals for observation of their obviously acute condition or regarded as severe cases of scarlet fever. They may even die without the correct diagnosis being made, and in such cases the laboratory has no help to offer.

Patients suffering from these severe forms of smallpox take to their beds early and stay there. It follows that they are less likely to spread infection to any but direct contacts than cases in the mild and moderate categories. The latter seem to spread their infection mainly *via* crust material and skin debris, i.e., after the outcrop of the modified focal

much delay in treatment, because the absence of such signs has been regarded as reliable evidence that the conditions suspected did not exist. Even though the clinical signs and symptoms persisted the negative radiological evidence obtained at the first examination has been allowed to dominate or confuse the outlook, for a time dependent upon the rapidity of progress of the disease: in some cases weeks, in others a year or more, and when a second examination has been requested, often the result of the calling in of a further consultant, the radiographs show characteristic evidence of extensive disease. This has occurred in many conditions, but more commonly in tuberculosis and malignant disease of bone. In some cases, however, the latent negative radiographic period is so long that even a second or third X-ray examination after intervals of weeks or months has failed to reveal positive evidence; notably in cysticercosis, some cases of bone tuberculosis and secondary metatases of malignant disease in bone. It is most important that periodical X-ray examinations be made, particularly in those cases in which the symptoms persist; certainly, immediately before any active "remedial" measures are employed a further careful radiological review of the case should be made.

The *reasons for this latent negative radiographic period* are:—

(1) Lesions must develop to a size which will permit of their recognition in the normal structures. No lesion can produce radiographic evidence until it has attained a size distinguishable by the naked eye. The size at which the lesions will be recognized is also dependent upon its position and whether or not it is associated with other lesions of a similar nature. Many miliary lesions in the lungs, whatever their nature, will be recognizable as such when they have acquired macroscopic size, but a few isolated lesions much larger in size may escape detection because of the variable pattern of the shadows of the normal lungs. These macroscopic lesions become recognizable by size only when they are of different density to the normal tissues in which they are developing, i.e., either more or less transparent than the latter.

(2) Lesions must produce a difference in density within the normal structures because a radiograph is but a register of the relative densities of all the structures traversed by the rays. Many lesions are of the same density as the normal tissues in which they are developing and so may attain great size and yet not register any evidence of their presence on the radiograph. The greater the contrast density produced by the lesion, the more ready its detection and the less contrast density given by the lesion, the longer will it escape radiological detection. Although of the same relative density, lesions may become visible by producing deformity of the visible contour of the structure in which they are growing or of adjacent organs: the radiologist is dependent upon such evidence for the detection of lesions such as gastric ulcer or carcinoma, brain tumour and the like.

The duration of the latent negative radiographic period.—The time required

EVALUATION OF THE NEGATIVE RADIOLOGICAL REPORT

By JAMES F. BRAILSFORD, M.D., Ph.D., F.R.C.P., F.I.C.S.

Radiologist, Queen Elizabeth Hospital, Birmingham.

IN patients with important items in their clinical history *or* those with obvious clinical signs and symptoms, X-ray examination often fails to show any departure from the normal. These cases are far in excess of those which show important, not necessarily spectacular, radiographic evidence and yet appear clinically to be sound. Such absence of correlation has been responsible for the unreasonable condemnation of the radiologist and radiographs by men who have not had the requisite training in clinical or radiographic work; for such men by the nature of their training avoid rather than seek cooperation; they have been taught on the basis of cases with well-established spectacular signs. Most of the radiographs shown to students at lectures and demonstrations, or illustrating textbooks, are of fully developed characteristic lesions ; from the very nature of things, illustrations indicating the earliest departure from the normal could not be used for teaching purposes, except for the person who has set out to study the problem and specialize. The early signs can only be appreciated by *routine daily examinations*, most of which show structures which are within the normal limits. Even the radiological features of the normal tissues require considerable study; since no two are exactly alike, the limits of the range show marked differences. Accepting this, it is necessary to realize that the early signs of departure from the normal may even evade the detection of the expert. But it is he who should investigate and explain his findings, either to the clinician who seeks his cooperation, or to students, e.g., during a ward class.

There is no ancillary service to medical and surgical science which is so much abused as radiology (Brailsford, 1945a). An account of the more common abuses have been published elsewhere. Because of the bad teaching of radiology to students there is a resultant failure to recognize what I have described (Brailsford, 1945b) as "the latent negative radiographic period", i.e., that period which elapses between the onset of clinical signs and symptoms, and the appearance of radiological evidence; and the "positive radiographic symptomless period", i.e., that period after the disappearance of clinical signs and symptoms, and during which the radiograph still shows departure from the normal.

THE LATENT NEGATIVE RADIOGRAPHIC PERIOD

The impression has been widely adopted that the onset of a lesion is immediately associated with the production of radiographic signs of such lesion. This is a fallacy which has been responsible for many errors in diagnosis and

trauma was severe and yet the X-ray appearances normal, the patient may be told that exercise and still more exercise is the best form of treatment. As most injured persons are anxious to get back to their duties, particularly when they have confidence in the surgeon, who warns them that some pain and disability must be expected whilst persisting in duties which are deemed essential by the surgeon for their recovery, work is continued even for a year or more in spite of much pain and increasing disability. When at last their confidence in the surgeon or rehabilitation officer breaks down and they seek other advice it may be found that the radiographs now show that the joint is disintegrated and beyond any hope of recovery. Rest of the joint giving pain or disability, with more careful radiological control at shorter periods to detect evidence of avascularity is the only way to prevent such disasters. Avascularity of the bone can be recognized radiologically by its relative density only when sufficient time has elapsed with the limb immobilized to permit of decalcification of the normal bone.

The destruction of the vascular supply to a fragment of bone results in avascular necrosis of the fragment. Such dead bone will ultimately be reconstituted by a gradual growth of vessels into it but so long as any portion remains avascular it will induce hyperæmia of the part and plasticity of the adjacent bone. Consequently, if the part is subject to function before complete reconstitution of the dead fragment, not only will the repair be delayed by repeated damage to the young vessels but pressure deformities of the plastic bone will develop and permanent disability will be caused. It may take up to four years before the dead fragment is removed. Prompt removal of the dead fragment would result in more rapid consolidation but when the stability of the part will be impaired, particularly in a young person, the longer immobilization would give the better ultimate result.

It may take upwards of several months before radiographs give supporting evidence of *tuberculosis* or secondary *carcinoma of bone*. The diagnosis has been missed on many occasions because the negative radiological evidence at one or perhaps two examinations has been regarded as excluding these conditions.

There are many other conditions which could be instanced in which there is a long latent negative radiographic period with ultimately definite and characteristic radiological evidence. To wait until the latter is present before adopting remedial measures is to rob the patient of the best chances of recovery. Too often, even in conditions in which the latent period is but a few weeks, because a radiograph taken in the early days of a patient with prominent symptoms is reported as negative, this evidence is taken as excluding the suspected condition and, although the clinical signs and symptoms persist or are aggravated, the call for a second X-ray examination is delayed well beyond the latent negative radiographic period and when it is made the radiographs show well-established disease with considerable destruction of the bones, often beyond the possibility of a good recovery.

for the production of radiographic evidence of so-called miliary lesions in the lungs is dependent upon the nature of the exciting cause and the rapidity and extent of reaction of the tissues to this cause. The inhalation of nitrous fumes may produce radiographic appearances in a few hours, but the miliary lesions due to tubercle bacilli may not be recognizable for several weeks after the clinical evidence has suggested their presence. The miliary lesions due to the inhalation of silica may not be sufficiently well developed to show for several years. Some lesions may never acquire a size which permits of their radiological demonstration; thus the cysts of the parasite in trichinosis (*Trichinella spiralis*) may not be calcified for ten years and even then they may not produce radiographic appearances which can be recognized, for they may be only just discernible by the naked eye in dissected specimens. The cysts of *Cysticercus cellulosæ*, which may measure $\frac{1}{3}$ by $\frac{1}{4}$ of an inch, cannot be detected by radiography until calcium has been deposited within, and this takes from five to ten years.

Whilst the clinical signs and symptoms of lobar *pneumonia* are followed within a few hours by radiographic evidence of reaction in the lung because this produces an alteration in the relative density of the lung, considerable breaking down of lung tissue can be present in emphysema or bronchiectasis without materially altering the radiographic appearances. The rapidity with which the tubercle bacillus produces radiographic appearances depends upon the relative virulence or resistance of the patient; the acute caseating broncho-pneumonic process produces radiographic evidence almost as readily as pneumococcal pneumonia, but the localized focus may take some weeks or months before its presence can be recognized by radiography.

The signs and symptoms of *pregnancy* are recognizable long before the radiograph will show evidence of it. It is rare to see radiographic evidence of the fœtus under nine weeks, and from then diagnosis depends upon the relative densities of the fœtal bones; if these are not normally ossified, as in osteogenesis imperfecta, the radiograph at full term may not reveal the fœtus as such. The signs and symptoms of acute osteomyelitis are recognizable ten to fourteen days before the radiograph shows any departure from the normal; to wait for radiological evidence before treatment would be to jeopardize the limb or life of the patient.

Following *injuries to bones and joints*, particularly those injuries which materially impair the vascularity, the radiographs may not show departure from the normal for weeks or months, although the clinical signs and symptoms have been continuous and might have warned the surgeon of the damage if he had not been influenced by the normal features of the part indicated by an X-ray examination soon after the injury. Radiographs taken following reduction of a traumatic dislocation of a joint may not show any departure from the normal for several weeks—the evidence provided by the radiograph after several months, may escape detection. Consequently the patient may be encouraged or even compelled to use the joint. Because the

trauma was severe and yet the X-ray appearances normal, the patient may be told that exercise and still more exercise is the best form of treatment. As most injured persons are anxious to get back to their duties, particularly when they have confidence in the surgeon, who warns them·that some pain and disability must be expected whilst persisting in duties which are deemed essential by the surgeon for their recovery, work is continued even for a year or more in spite of much pain and increasing disability. When at last their confidence in the surgeon or rehabilitation officer breaks down and they seek other advice it may be found that the radiographs now show that the joint is disintegrated and beyond any hope of recovery. Rest of the joint giving pain or disability, with more careful radiological control at shorter periods to detect evidence of avascularity is the only way to prevent such disasters. Avascularity of the bone can be recognized radiologically by its relative density only when sufficient time has elapsed with the limb immobilized to permit of decalcification of the normal bone.

The destruction of the vascular supply to a fragment of bone results in avascular necrosis of the fragment. Such dead bone will ultimately be reconstituted by a gradual growth of vessels into it but so long as any portion remains avascular it will induce hyperæmia of the part and plasticity of the adjacent bone. Consequently, if the part is subject to function before complete reconstitution of the dead fragment, not only will the repair be delayed by repeated damage to the young vessels but pressure deformities of the plastic bone will develop and permanent disability will be caused. It may take up to four years before the dead fragment is removed. Prompt removal of the dead fragment would result in more rapid consolidation but when the stability of the part will be impaired, particularly in a young person, the longer immobilization would give the better ultimate result.

It may take upwards of several months before radiographs give supporting evidence of *tuberculosis* or secondary *carcinoma of bone*. The diagnosis has been missed on many occasions because the negative radiological evidence at one or perhaps two examinations has been regarded as excluding these conditions.

There are many other conditions which could be instanced in which there is a long latent negative radiographic period with ultimately definite and characteristic radiological evidence. To wait until the latter is present before adopting remedial measures is to rob the patient of the best chances of recovery. Too often, even in conditions in which the latent period is but a few weeks, because a radiograph taken in the early days of a patient with prominent symptoms is reported as negative, this evidence is taken as excluding the suspected condition and, although the clinical signs and symptoms persist or are aggravated, the call for a second X-ray examination is delayed well beyond the latent negative radiographic period and when it is made the radiographs show well-established disease with considerable destruction of the bones, often beyond the possibility of a good recovery.

THE POSITIVE RADIOGRAPHIC SYMPTOMLESS PERIOD

This period may exist for but a few days after the disappearances of clinical signs and symptoms, as in pneumonia, but in a number of conditions radiological evidence of past disease persists for the remainder of an apparently healthy life. Generally speaking the less the destruction during the active phase the less the residual radiographic evidence. Lesions which tend to calcify are those which show the most persistent radiographic evidence. The cysts of animal parasites, (cysticercus cellulosæ, echinococci, trichina, filaria, dracunculus, schistosoma), as has been shown, may not be recognizable during the active phase of their existence when the most important symptoms are caused, but once calcified they produce radiographic evidence which will persist throughout the remainder of the patient's life, usually unaccompanied by any symptoms. The same can be said of the calcified fibroid and the overlooked fœtus which is transformed into a lithopædion.

Some inflammatory lesions leave no trace, but those which show calcification or abnormal ossification, such as osteomyelitis and tuberculosis, may persist as healed lesions always recognizable by radiography; other cases exhibit periodic recrudescence. In the early stage of recrudescence, although the clinical signs are prominent, the radiograph will not give any indication of anything but a healed lesion, i.e., again there is a latent negative radiographic period and it is necessary to wait for some time before radiological evidence of the reactivity of the lesion can be obtained.

Two sources of error are possible from this positive radiographic evidence. The spectacular appearance of the healed lesion may be discovered accidentally during a routine examination, as in mass radiography of the chest or following radiography for an injury, and be responsible for surgical interference or prolonged investigation, although the patient shows no signs or symptoms. On the other hand, the detection of radiological evidence of calcified or consolidated foci may cause the observer to regard the lesions as healed and to discount the symptoms of which the patient complains, particularly if the question of compensation in any form has to be considered, or if the recent radiographs show no change from others taken during the quiescent period.

The latent negative radiographic period of reactivity of an old lesion or of a secondary or tertiary infection may be imposed on a patient whose radiographs show evidence of an old lesion, i.e., one showing the positive radiographic symptomless period. There is always a danger that the radiographic evidence of an old healed lesion will be allowed to dominate the treatment although the patient may be showing clinical signs and symptoms. For instance, although the X-ray examination may show calcified cysticerci this is no evidence that a more recent infestation has not occurred. The radiographs at the site of a recent injury may show for a time only evidence of an old lesion—I have observed this in a patient who had sustained a recent

injury to the wrist. The radiograph showed an old ununited fracture of the scaphoid with rounding off of the fractured surfaces but no signs of recent injury; it was only after a month that further radiographs showed that the recent injury had in fact rendered one fragment avascular and that considerable osteoporosis had been produced in the interval. The radiographs of bones which have been involved in osteomyelitis may show only evidence of the old disease for a week or so after the patient has exhibited clinical evidence of a recrudescence; nor must it be forgotten that malignant metaplasia may occur in any of the lesions of the osseous dystrophies, simple cysts and tumours, or the sites of old injuries. For a time the radiographs will show but the evidence of the old lesions although careful examination of the clinical evidence may indicate that a change has taken place. It is necessary to wait for a variable period, depending upon the rapidity of the malignant growth, for the radiological evidence to indicate that disintegration or other change is in progress. But it is in tuberculosis of the lungs that faulty interpretation of the radiographic appearances is most often met with. This is a serious matter, because it is now common practice to dispense with investigations of the clinical history and conditions and depend upon the radiograph for evidence of active disease and if it is not present to ignore what appears to be old calcified foci: indeed the directors of official mass radiographic units are told by the Ministry's advisers to ignore these calcified lesions. As any patient with a calcified primary focus or a post-primary calcified lesion may at any time become reinfected and for a time fail to show radiographic evidence of this re-infection, i.e., the latent negative radiographic period of reinfection, such advice may well lead to such delay in treatment that recovery may be impossible and in the interval the unsuspected disease may be disseminated, the more readily because at a radiographic examination the patient was declared free from infection.

SUMMARY

Radiological examination, although important, is but a specialized part of a complete clinical examination. Used alone, without investigation of the clinical history signs and symptoms, it may be very misleading, for some patients may have important features in their history and/or prominent clinical signs and symptoms yet no radiographic evidence of departure from the normal, whilst others without signs and symptoms may have obvious spectacular radiographic signs. The significance of these apparent discrepancies can only be fully appreciated when there is reasonable cooperation between clinician and radiologist in their investigation of patients. Radiology is not, and ought not to be used as, a quick substitute for the adequate and more time-consuming clinical investigation.

References

Brailsford, J. F. (1945a): *Brit. J. Radiol.*, **18**, 249.
——, —— (1945b): *Proc. roy. Soc. Med.*, **38**, 550.
——, —— (1945c): *Lancet*, ii, 808.

OPHTHALMIC PROBLEMS IN INDUSTRY

By JOSEPH MINTON, F.R.C.S.

Ophthalmic Surgeon, Hampstead General Hospital; Queen Elizabeth Hospital for Children; Assistant Ophthalmic Surgeon to the West End Hospital for Nervous Diseases; Ophthalmologist to the Department of Industrial Ophthalmology, Royal Eye Hospital, London.

THIS recent war has given a great impetus to the development of the industrial medical service. At the same time, the problem of selection of employees for the right job is being given greater attention and many industrial medical officers are asking ophthalmologists to advise them on visual standards required in industry.

Modern industry is capable of employing men and women with all grades of vision, from grade 1 with the highest degree of vision to the partially and totally blind. The standards of vision required should not be rigid, but should vary according to the jobs assigned to the workpeople in the factory. Vision is only one of the factors necessary in the make-up of a skilled worker. High intelligence and experience often counterbalance the handicaps which arise from poor visual acuity. In the selection of the right man for each job, the total physical and mental make-up should be the guiding principle. For all workers in industry the use of glasses should present no handicap. It is therefore suggested that visual standards should refer to the worker's vision corrected, if necessary, with glasses.

VISUAL GROUPS

Industrial medical officers, factory surgeons, welfare officers and others need general guidance on visual standards. I have therefore drawn up a rough scheme which has been found to be of practical use as a guide.

It is suggested that workpeople can be divided into five visual groups:—

Group 1: To this group belong all individuals having 6/6 or 6/9 vision in each eye, and also those having 6/6 in one eye, and not less than 6/36 in the other eye. Workpeople belonging to this group are fit for all occupations, including fine close work.

Group 2: This group includes all individuals having not less than 6/12 vision in each eye, and also having 6/12 vision in one eye and not less than 6/36 in the other. Workpeople with this grade 2 vision are fit for all industrial occupations in engineering industries, except the close work mentioned above. Grade 2 is also sufficient for all clerical work and for the driving of vehicles.

Group 3: This group covers all the one-eyed people who have 6/6, 6/9, or 6/12 in the good eye and less than 6/36 in the other eye, or who have one blind eye.

I am often asked by one-eyed people what jobs they should take up. I consider that a one-eyed person with 6/6 in the good eye is fit for any occu-

pation, even that which requires fine close work. The one-eyed who have 6/9 or 6/12 vision can be engaged in most trades and industries, except occupations such as coal mining and certain operations in the engineering trades, such as hammering, chipping, turning, milling, which present a greater danger of injury to the eyes.

Group 4: To this group belong the workpeople who have 6/24 vision in each eye, or 6/24 in one eye and 6/36 in the other eye. People with grade 4 vision can be employed in all outdoor occupations.

Group 5: To this group belong the blind and partially blind, and it can include all individuals with less than 6/36 vision in each eye.

The National Institute for the Blind has issued several pamphlets dealing with the employment of the blind. They show how, since the beginning of the war, the blind and partially blind have been employed in hundreds of industrial occupations.

It should be remembered that visual standards laid down for any particular job should not be rigid, and that the general experience and mentality of the worker should be taken into account when selecting an employee for any particular job.

VISUAL STANDARDS IN INDUSTRY

Grade	Degree of vision	Suitable occupation
Grade 1 vision ..	One eye 6/6 Other eye 6/36 or better, or 6/9 in each eye	Workers in this group are fit for all occupations including fine close work
Grade 2 vision ..	One eye 6/12 Other eye 6/36 or better	This group is fit for most occupations in engineering industry and clerical work. Fit to drive motor vehicles
Grade 3 vision ..	All one-eyed people with not less than 6/12 in good eye	One-eyed people are fit for most occupations. The safety of the good eye must always be ensured. Coal mining, hammering, chipping and drilling should not be carried out by one-eyed people
Grade 4 vision ..	One eye 6/24 Other not less than 6/36	Fit for outdoor occupations, carpentry, gardening, dock labour
Grade 5 vision ..	All blind and partially blind less than 6/36 each eye ·	See pamphlet issued by the National Institute for the Blind

These visual standards are based on the vision of the worker, corrected if necessary with glasses.

SPECIAL PROBLEMS

Special visual problems which are of interest in industry are:—

(1) The selection and allocation of jobs to juveniles
(2) Myopia
(3) Fine close work

The Factories Act of 1937 provides that juveniles employed in factories should be examined by the factory surgeon and an eyesight test carried out. At present the factory surgeon has few or no facilities for examining the juvenile's eyesight. It is essential, in my opinion, to use Snellen's test type at twenty feet when vision is tested. Should the vision of the juvenile be less than 6/12 in each eye, he should be referred to an ophthalmic surgeon for an examination.

A report by an ophthalmic surgeon of the juvenile's vision, corrected if necessary with glasses, would be of real value to the factory surgeon in deciding the suitability of that juvenile for any particular job under consideration. It would also be advisable that the factory surgeon should not allow one-eyed persons to be engaged in occupations which present danger of injury to the eyes, such as those outlined above.

Myopia.—The question of employment of myopes in fine close work has engaged the attention of ophthalmologists for several generations. In the past, many ophthalmologists were of the opinion that close work caused a deterioration of the sight of myopes. They were advised not to take up clerical work, needlework, or any other form of fine close work. Modern views of progression of myopia are at variance with the old theories. I am of the opinion that myopes with good vision in each eye (6/6 or 6/9) should not be advised to turn down clerical work or any other type of fine close work when choosing their careers.

Some educational authorities have refused scholarships to adolescent myopes with 6/6 or even 6/5 vision in each eye, if their myopia exceeds four or five dioptres. In my opinion such a course of action is unjustifiable.

Fine close work.—Fine work at close range presents a special problem in industry. The radio valve industry, electric lamp inspection and manufacture, fine weaving and silk hose manufacture, require a constant accommodation effort and convergence to a greater degree than does ordinary clerical work. In the selection of workers for these jobs, greater attention should be paid to a full investigation of vision. The visual acuity required is 6/6 or 6/9 in each eye. The muscle balance and binocular vision should also be investigated. A Maddox wing can be used for measuring the muscle balance of the eyes for near vision, and a Worth's amblyoscope is a convenient instrument for estimating the degree of binocular vision (fusion, stereopsis and convergence). Both instruments are small and cheap.

Industrial medical officers are not usually fully acquainted with the details and interpretation of muscular imbalance. It would therefore be advisable that an investigation by an ophthalmic surgeon be carried out on all indivi-

duals engaged or likely to be engaged in such work. As a general guide it might be recommended that employees engaged on very fine close work should have no hyperphoria. The exophoria or esophoria must not be greater than five prism dioptres. They should have good stereoscopic vision as well as a corrected visual acuity to 6/6 or 6/9 in each eye. It is interesting to note that one-eyed workers with 6/6 vision in the good eye can continue working comfortably in occupations involving fine close work. Such careful selection of workers for fine close work should have the assistance of an orthoptist, who might carry out treatment of individuals with small degrees of muscle imbalance and poor stereoscopic vision, but who are otherwise fit and willing to do such work.

Young men and women with a high error of refraction (latent hypermetropia) will often have 6/6 vision but will suffer from headaches if engaged on close work. In all such cases a routine examination by an ophthalmic surgeon would lead to a correction of refractive errors and of muscle imbalance, and thus would prevent headaches and eye-strain from which these workers often suffer.

As a general rule it can be stated that individuals with refractive errors, if properly corrected with glasses, suffer no discomfort when engaged on close work. Older workers wearing glasses to correct their presbyopia are just as efficient as younger workers.

The selection of workers for suitable jobs is one of the great problems to be solved after this war. With the cooperation of the industrial medical officers, a great deal may be accomplished.

References

Bourne, L. B. (1944): "Selection of Employees for Fine Close Work" (Paper read to the Industrial Welfare Society).
Mann, I., and Archibald, D. (1944): *Brit. med. J.*, i, 387.
Minton, J. (1939): *Trans. Ophthalmol. Soc.*, **59**, part 1.
—— (1945): *Brit. J. Phys. Med. Hyg.*, **8**, 112.
National Institute for the Blind (1943): "Skilled Hands of the Blind;" and other pamphlets dealing with the employment of the blind.
Weston, H. C., and Adams, S. (1927): *Indust. Fat. Res. Brd. Rep.*, no. 40.
—— (1928): *Ibid.*, no. 5 and 49.

SOME DERMATOLOGICAL FALLACIES

By A. J. AMBROSE, L.M.S.S.A.

If Sherlock Holmes were writing this article, he would say "elementary, my dear Watson", but Michael Angelo said that "perfection consisted of trifles and that perfection was no trifle", and I am convinced that those who are beginning their studies in dermatology would be well advised to avoid the following mistakes, all of which I have encountered in practice.

DIAGNOSIS

Scabies.—When sulphur was the remedy of choice, dermatitis was set up by too prolonged treatment. Even since benzyl benzoate has to a great extent supplanted sulphur, dermatitis produced in the same way is occasionally seen. Scabies between the fingers is frequently masked and mistaken for eczema.

Lupus vulgaris.—The usual site for lupus vulgaris is the nose. When it occurs on unusual parts of the body, such as the arm, it may easily be mistaken for some other skin condition.

Lupus erythematosus, when present on the ears, may easily be mistaken for tertiary syphilis, and when on the hands and feet for Raynaud's disease.

Impetigo is frequently treated with too strong an application, for instance, ammoniated mercury is often said to be unsuitable because the rule laid down by the late Sir Norman Walker has not been observed: "Do not use it stronger than 5 grains to the ounce". Other mistakes in treating impetigo are: (1) to use an ointment when a paste is preferable where and when there is exudation; (2) to treat impetigo with the same drug for too prolonged a time, experience showing that frequent change of treatment not only avoids sensitization but also gets better results. Sulphonamides locally are seldom necessary but if used should not be employed for longer than five days, to avoid sensitization and dermatitis.

Granuloma annulare.—I have seen this condition mistaken and treated for ringworm on the back of the hand.

Primary sore.—I have seen a primary sore overlooked because it appeared on the face.

Pediculi capitis can easily be overlooked if the social position of the patient causes the medical man to forget that clean people can be infected by contact with dirty people. I attended a lady for this trouble who apparently was infected whilst travelling in a first-class railway carriage and who developed a mild dermatitis of the neck because, in her anxiety to get rid of the scourge, she kept on rubbing in the remedy (benzyl benzoate) for too long a period.

Erythema multiforme.—I have seen this condition mistaken for chilblains.

Lichen urticatus.—I have seen the bullous form mistaken for mild smallpox. It is more commonly mistaken for chickenpox.

Pityriasis rosea.—I have seen this diagnosed as syphilis.

Smallpox.—The mild form of smallpox can easily be mistaken for chickenpox. I have avoided making this mistake by getting into the habit of looking to see whether the pocks were more numerous on the face or on the trunk and detected two cases of smallpox which clinically looked like chickenpox because of this fact. The face and the peripheral parts of the limbs are relatively more involved in smallpox than in chickenpox. There are of course other points of difference but I can recommend this simple differential test. It should also be remembered that there is one very rare form of vaccinial eruption which closely resembles smallpox, except that there is little or no fever and the patient is not ill.

Sporotrichosis.—This disease, which shows itself at first by the presence of elastic swellings, is caused by chickens or other birds pecking the exposed parts, such as ears, hands and face of their keepers, with beaks contaminated by decaying vegetable matter. I saw a case which had been diagnosed by a colleague as chilblains. Although cited in books as a rare disease it is quite probable that the complaint is more prevalent than is supposed, and I draw attention to it so that it may not be overlooked.

Schamberg's disease.—I have seen only one case of Schamberg's progressive pigmentary dermatosis in forty-five years, but I mention it because when I was physician to St. Joseph's Hospice, Hackney, I was asked to see a patient suffering from this complaint whose legs were so greatly discoloured that her medical attendant had sent her in as a case of "double gangrene"!

Syphilitic necrosis of the skull.—During my term of office at St. Joseph's Hospice I also saw a case of syphilitic necrosis of the skull which had been diagnosed by a provincial M.O.H. as tuberculosis of bone.

Erythema ab igne may be present in stokers, blacksmiths, and glass blowers, but is common in women who are addicted to the habit of sitting with their legs too close to the fire. I mention it because an assistant of mine, not familiar with the condition, so alarmed one of my patients that she rushed up to me screaming "I won't have to have both my legs cut off, will I?"

Lichenification, especially at the back of the neck in women, might also be mentioned as I have seen cases which had persisted for two years, the irritation of which had caused the sufferers to have sleepless nights and which cleared up in a month, either by the local application of undiluted solution of coal tar or by fortnightly ½ pastille doses of X-rays and attention to the accompanying dandruff of the scalp.

Rodent ulcer must not be overlooked, as I have seen it done in scabbed eczema, when scabs near the eyes and nose sometimes cover a rodent ulcer.

The commonest and perhaps the greatest mistake of all is *to not examine the scalp in every case of skin trouble.* Seborrhœa and its many and varied manifestations start in the scalp, and the diagnosis and treatment of many cases of skin diseases are to be found in the scalp and the accompanying dandruff.

TREATMENT

Calamine lotion used in cases in which the skin is dry when calamine liniment (oily calamine lotion) would have been much more effective. This is one of the most common mistakes I have encountered.

Glycerin is an irritant to some skins and it is safer to use it as glycerin of starch or glycerin of tragacanth. In weeping eczema, however, glycerin is of great value used as a starch pack :—

℞					
Glycerin of lead acetate	..	..	..	20 minims (1·2 c.cm.)
Olive oil..	..	..	..	..	30 minims (1·8 c.cm.)
Starch powder	..	..	..	..	90 grains (6 gm.)
Zinc oxide	..	..	..	..	120 grains (8 gm.)
Soft paraffin	..	..	..	..	120 grains (7 c.cm.)
Hydrous wool fat	..	..	..	to 1 ounce (28·4 c.cm.)

Bockhart's paste (equal parts of talc, oxide of zinc and glycerin and water) is suitable in cases of eczema of the anal region and legs and is far better than more greasy applications.

Tar can lead to mistakes in its use as also in its non-use. Beginners in dermatology would be well advised to avoid tar in acute skin troubles and to be sure to use it in chronic cases, and when using it to start with a low concentration.

Rubella and scarlet fever are sometimes difficult to differentiate, but the rapid pulse in the latter and the enlarged occipital and posterior cervical glands in the former should be remembered in all these cases.

Sycosis.—A common mistake is to use too strong treatment under the impression that because of the condition being due to infection strong antiseptics are necessary, whereas in actual practice it is found that these cases need soothing treatment in the acute phase.

X-ray advised for superfluous hair.—This is a great mistake as its use may cause grave damage to the skin.

X-rays in impetigo.—This again is a mistake as its use may cause a flare-up of eczema.

Ultra-violet light.—The indiscriminate use of ultra-violet light in the treatment of eczema is a mistake. It is only certain types of eczema, in which there is probably a deficient calcium content in the skin, that do well with judicious actinotherapy.

Sulphonamides are rarely needed and, as they may cause sensitization and dermatitis, their use should be withheld until simpler measures have been tried.

Keratoses, sometimes referred to as warts, on the back of the hand should be regarded as malignant and treated by excision. As these growths are of slow growth they do very well if treated early, but I saw one case which had a fatal termination because the real nature of the disease was recognized too late.

Dermatitis caused by plants treated as eczema.—One of my patients was treated at a London skin hospital for eczema and had no further trouble when she destroyed a lily pond, which was the real cause of her dermatitis venenata.

THE EARLY RECOGNITION OF DISEASE

IX.—THE COMPLICATIONS OF PREGNANCY

By W. C. W. NIXON, M.D., F.R.C.S., F.R.C.O.G.

Surgeon, Soho Hospital for Women, London; Obstetric Consultant, London County Council.

CERTAIN symptoms during pregnancy are often taken for granted. Yet these so-called minor manifestations may herald really grave complications. In early pregnancy the most common complaints are vomiting, frequency of micturition, vaginal discharge and hæmorrhage.

VOMITING

Mild vomiting.—It has been estimated that 30 to 40 per cent. of pregnant women suffer from nausea with or without vomiting. There is no satisfactory explanation for this. The idea that the origin is psychological cannot explain all these cases. A woman may have been suffering from amenorrhœa for a long time and then become pregnant without realizing it. She will start vomiting. There cannot be a psychological element in this instance. Every system has been blamed—alimentary (stomach and colon), endocrine, nervous. Gastric analysis sometimes reveals a diminished amount of HCl. In such a case alkalis make the condition worse; vomiting may cease abruptly with the administration of the acid. After the twelfth week nausea or vomiting usually disappears in the majority of pregnant women. The placenta is then a fully functioning endocrine gland. When vomiting is persistent it is advisable to do a vaginal examination. A few cases have been seen in which there has been a dramatic cessation of vomiting after replacing a retroverted uterus.

Pernicious or toxic vomiting.—There are a few pregnant women who at an early date vomit excessively. They are able to retain neither fluid nor solid food. There are others who in the beginning of pregnancy are not unduly disturbed by the intensity of the vomiting but who gradually sink into the category under discussion. In the grave case the clinical picture is typical. It is one of dehydration. With eyes sunken, skin inelastic, urine diminished, a low blood pressure, a raised temperature and pulse, diminished knee-jerks and, finally, nystagmus (Wernicke's encephalopathy), the patient deteriorates and dies. The really severe and intractable type of vomiting is rare. Unfortunately it is difficult in the early stages for the medical attendant to predict which woman may find herself later in the serious category described above. It is incumbent upon the attendant to institute really rigorous treatment, especially institutional, whenever vomiting is refractory to the simple methods of therapy. Daily weighing, blood pressure estimation, urine analysis and output are prerequisites in the management of such a case. Examination of the discs should be done periodically, and at

the earliest sign of retinal hæmorrhage the pregnancy should be terminated. Even so, such interference may be too late to avert a fatal result.

The presence of icterus used to be considered of especially grave significance. With the high incidence of infective hepatitis the possibility of the jaundice being due to this disease needs to be borne in mind. Acute yellow atrophy is fortunately rare and in the past it has been mistaken for infective hepatitis. In most cases of the latter, pregnancy can proceed uninterruptedly. When the so-called toxic type of hyperemesis gravidarum is complicated by jaundice then the patient needs special care. It is only by careful evaluation of the early symptoms and signs and by termination of pregnancy that death can be averted.

FREQUENCY OF MICTURITION

Many women complain of frequency early in pregnancy. This may be mechanical in origin or due to an infection of the urinary tract. When this complaint is pronounced a catheter specimen should be examined bacteriologically. In this way an early diagnosis of *B. coli* infection can be made. This organism can be present in the absence of the typical clinical picture of pyelitis. Treatment should be instituted forthwith.

VAGINAL DISCHARGE

Physiological.—Early in pregnancy it is natural for women to complain of a sensation of moisture. This is due to the increased secretion of the cervical glands and hyperæmia.

Pathological.—When the discharge becomes excessive, stains the clothes, and is offensive and irritating, a full bacteriological investigation of the genital tract is indicated. Swabs for culture and smears should be taken from both the urethra and cervix. A hanging drop of the discharge from the fornix pool should be examined under the microscope. This simple procedure will reveal the Trichomonas organism which is a frequent cause of severe vaginitis. Monilia vaginitis is another type of infection that is more commonly found in pregnancy. Burning and itching may be severe. In order to identify the fungus, scrapings should be taken from the white patches, placed on a slide and stained with methylene blue.

HÆMORRHAGE

This is one of the major contributory factors to maternal mortality. A useful classification is that adopted by Montgomery (1945), namely, "intrinsic" or "extrinsic". Into the category of intrinsic fall abortion, ectopic gestation, hydatidiform mole, placenta prævia, premature separation of the placenta. Extrinsic are such conditions as lesions of the cervix— erosion, polyp or carcinoma—varicosities of the vagina or vulva, and the like. These are diagnosed by speculum examination. The introduction of a bi-valve vaginal speculum can be done without causing pain and without in any way dislodging the pregnancy. An erosion can only be diagnosed by

viewing the cervix. Every pregnant woman complaining of discharge or bleeding should have a speculum examination.

During the first trimester.—Abortion is the most frequent reason for bleeding during the first three months of pregnancy. The difficulty is to know when a threatened abortion has become an inevitable abortion without doing a vaginal examination. It is surprising how some women can have continuous and excessive bleeding and yet continue their pregnancies. The intensity and frequency of uterine contractions can be a guide as to when a threatened abortion has become an inevitable abortion.

If there is any doubt a vaginal examination should be done. Just as with the speculum so with the fingers, an examination done properly and gently does not disturb the pregnancy. The finding of the cervix effaced, the os dilated and a soft mass just within the cervical canal makes the diagnosis obvious. Cases are known of so-called threatened abortions, which have been wrongly diagnosed as such, with the patient lying for days in bed and having progesterone injections. A timely vaginal examination has revealed the true condition, namely, incomplete or complete abortion. The urine test (Zondek-Ascheim or Friedman) is not always helpful, since it may remain positive for some days after the death of the ovum. However, urine pregnandiol estimation is of value. This test does help in predicting which pregnancies will abort with certainty and which will continue for the full period of gestation. When pregnandiol excretion is diminished or ceases altogether then the abortion is inevitable.

Ectopic gestation.—This is one of the most difficult conditions to diagnose and Cope's (1946) reference to Grandin's observation is apposite: "The man who suspects every woman of having the condition is the man who is least liable to err in diagnosis." History is helpful. On careful inquiry it is usually found that menstruation has been irregular. Bleeding is constant and usually not excessive. It is punctuated with attacks of spasmodic lower abdominal pain. Compared with an abortion this bleeding is less and the pain, usually more acute, precedes the bleeding. Of course, when there is tubal rupture with severe bleeding the picture is typical and the diagnosis obvious. But this type is rare. It is the subacute or chronic (hæmatocele) type that is seen more commonly. In this type I have found (1937) puncture of the posterior fornix a most useful aid. After the usual antiseptic preliminaries, a self-retaining speculum is passed and the posterior lip of the cervix steadied with a volsellum forceps. A large-bore needle with 10 c.cm. syringe attached is inserted through the posterior fornix into the pouch of Douglas. If the needle is kept close to and parallel with the posterior wall of the cervix there is no danger of entering the rectum. Withdrawal of blood confirms the presence of free blood in the pelvic cavity. With hæmatocele the fluid withdrawn is brownish-black in colour.

Hydatidiform mole.—This complication manifests itself more commonly in the second trimester of pregnancy. Pregnancy will have been diagnosed at an early date but after a few weeks or months a blood-stained discharge

will be complained of. At times the bleeding may be brisk. The uterus enlarges rapidly and the concomitant uterine distension may be associated with severe pain. It is not the invariable rule for the uterus to be larger than the period of amenorrhœa. Abdominal examination does not reveal the presence of a fœtus. On vaginal examination internal ballottement is absent. Radiography will not show a fœtus. The Zondek-Ascheim test is positive, even with marked dilution of the urine.

HÆMORRHAGE LATE IN PREGNANCY.—Ante-partum hæmorrhage—bleeding during the third trimester—is most commonly due to (1) placenta prævia, or (2) premature separation of the placenta (accidental hæmorrhage).

(1) *Placenta prævia.*—The bleeding is not usually accompanied by pain. During this period of pregnancy a woman may casually mention that she has noticed only slight "spotting". Even with this slight amount of bleeding placenta prævia should be suspected. On abdominal examination a malpresentation may be found or the presentation is a vertex but high and difficult to fix in the brim. On auscultation the placental souffle may be heard just above the pubis.

The passage of a vaginal speculum will help to exclude conditions that are "extrinsic", namely, lesions of the cervix and vagina. On the other hand, digital examination is contraindicated unless it is done in the operating theatre and the examiner is prepared to proceed with a Cæsarean section operation if such is indicated.

In America, considerable investigation has been done on the X-ray diagnosis of placenta prævia. By the use of a special soft-tissue technique and lateral plates the position of the placenta can be seen. It is claimed that by this method it is possible to detect the situation of the placenta, when it is normally situated, in about 97 per cent. of the cases. Moir (1944) has indicated some fallacies of soft-tissue placentography. Opinions are divided as to the value of cystography for the early diagnosis of placenta prævia.

(2) *Premature separation of the placenta.*—The bleeding in this complication is often accompanied by uterine pain and in this way differs from that in placenta prævia. There may or may not be albuminuria with hypertension. In most cases the hæmorrhage starts as a slight loss and remains so. Fortunately, the fulminating type of abruptio placentæ is rare. The onset is sudden but œdema may have been present some time before. Diminution of urinary output indicates an impending renal catastrophe.

ANÆMIA IN PREGNANCY

Every pregnant woman should have her Hb. estimated when she is first seen. In clinic practice the Wassermann reaction is now done as a routine. The same should apply to the Hb. and Rh factor. By this simple test, not only is nutritional anæmia discovered, but also anæmia of the macrocytic type. A lowered Hb. calls for a complete blood test and in this

way the more serious types of anæmia will be detected. Ideally, every pregnant woman should have her Hb. and red cells estimated at the first visit and repeated at the thirty-sixth week. At this latter date the physiological hydræmia of pregnancy must be taken into account.

TUBERCULOSIS AND PREGNANCY

The easiest and most reliable method for early detection of pulmonary tuberculosis in pregnancy is by chest screening. Since 1943 this has been an established practice in the antenatal clinic of Paddington (L.C.C.) Hospital, and Frank and Jacobs (1944) have reported their findings in 1,125 women. Active tuberculosis requiring immediate admission was found in 0.5 per cent.; possibly active, requiring close observation, in 0.2 per cent.; and probably inactive or not definite tuberculosis, but requiring observation, in 0.8 per cent. Since 1943 or 1944, a total of about 4,500 expectant mothers has been screened: the results will be published shortly. This practice should be made obligatory in all antenatal clinics. It is quite economical, does not require much organization and is a certain way of detecting pulmonary disease early in pregnancy.

ABDOMINAL PAIN IN PREGNANCY

Abdominal pain is sometimes an early symptom of a serious complication. A pregnant woman complaining of such should be immediately and fully investigated. Some of the more common complications have already been indicated. Fahmy (1944) has given an admirable summary of causes of abdominal pain ; some of them are rare. In the first trimester he includes ectopic gestation, iliac fossa pain, ovarian hæmorrhage and angular hæmorrhage; in the second trimester, pyelitis, acute hydramnios, hydatidiform mole, ureteral spasm, appendicitis, fibroid and ovarian tumours and adhesions; in the third trimester, abruptio placentæ, rupture of the uterus, hæmatoma of the rectus muscle, costal margin pain, rupture of a vein in the uterine wall, torsion of a gravid uterus, gall-bladder pain and pain of orthopædic origin.

Some of the more common conditions will be discussed in detail.

Pyelitis.—The pain is more usually felt on the right side and may be localized to the region of the renal pelvis or in the line of the ureter. The attack may start with a rigor. The temperature is higher than in appendicitis. Frequency of micturition and dysuria may be complained of but are not invariably present. Whenever a pregnant woman complains of acute abdominal pain a catheter specimen of urine should always be examined bacteriologically. By routine examination of an ordinary specimen of urine in the early months, pus may be detected before the onset of symptoms. A catheter specimen should then be taken. Persistence of pyuria may be indicative of some abnormality in the urinary tract, such as calculus or tuberculosis. Pyelography and cystoscopy are then essential.

Ovarian cyst.—A small ovarian cyst in the pouch of Douglas may be discovered on routine vaginal examination early in pregnancy. It is only by

such an examination that it will be discovered before the onset of serious complications. For this reason every pregnant woman should be examined vaginally at the second or third interview. With torsion there is acute abdominal pain accompanied by vomiting. The vomiting and pain begin simultaneously and the synchronization of these two dominant symptoms is a point that differentiates the condition from appendicitis.

Fibroid tumour.—When a woman is known to have a fibroid before her pregnancy the attendant will naturally be on the watch for complications. The most common complication is red degeneration (necrobiosis). The patient will complain of pain at the site of the tumour and tenderness will be marked. As in the case of an ovarian cyst, so a pedunculated fibroid may twist. Again pain and vomiting will begin together.

General surgical conditions.—A pregnant woman can suffer just as readily from appendicitis, perforated gastric ulcer or cholecystitis as her non-pregnant sister. What pregnancy does is to make the diagnosis more difficult by masking symptoms and signs. For instance, it is very easy to blame the pregnancy for the vomiting and other alimentary disturbances. In appendicitis, particularly when the appendix is concealed by the bulky uterus, it is not easy to elicit the classical local signs in the early phase of the disease. It has been found helpful to alter the posture of the patient when palpating the abdomen. Instead of the dorsal she should adopt the left lateral or even the genu-pectoral position. The tips of the fingers can then reach parts that were inaccessible when the patient was lying on her back.

TOXÆMIA OF PREGNANCY

It is now accepted that a raised blood pressure may be the earliest sign of this disease. A rise of blood pressure may be noted some weeks before albumin appears in the urine. It is essential that the medical attendant should take the blood pressure every time a pregnant woman is seen. The case may be one of essential hypertension, in which condition the pregnancy may proceed to term without the development of any other signs.

Oedema is a finding of real significance and should always be looked for. With even slight œdema of the ankles or hands the conjunctivæ should also be examined. Subconjunctival œdema—tears that do not run—is a sign of generalized œdema. Œdema is often a precursor of a rise of blood pressure or of albuminuria. It is for this reason that some authorities advocate weighing of the expectant mother at frequent intervals so that hidden œdema may be detected early.

References

Cope, V. Z. (1946): "The Early Diagnosis of the Acute Abdomen," 9th edition, London. 182.
Fahmy, E. C. (1944): *Edin. med. J.*, **51**, 229.
Frank, R., and Jacobs, A. L. (1944): *Brit. med. J.*, i, 394.
Moir, C. (1944): *Amer. J. Obst. Gynec.*, **47**, 198.
Montgomery, T. L. (1945): *Surg. Clin. N. Amer.*, **25**, 1408.
Nixon, W. C. W. (1937): *Brit. med. J.*, ii, 579.

REVISION CORNER

This section is devoted to short articles in which experts summarize modern treatment and clinical procedures, particularly for the benefit of general practitioners who have returned from the Forces.

DYSPHAGIA

Difficulty in swallowing may be classified either anatomically or by the common causes at different ages. Omitting the oral conditions, such as stomatitis, tonsillitis, mumps, and the like, the important causes can be grouped thus:—

Upper œsophageal dysphagia (Pharyngo-œsophageal)	Syndrome with iron deficiency anæmia
	Carcinoma (post-cricoid)
	Pharyngocœle
	Diphtheria
	Retro-pharyngeal abscess
	Syphilitic stenosis
	Myasthenia
	Bulbar palsy
	Vallecular dysphagia
Mid-œsophageal dysphagia	Carcinoma
	Extrinsic pressure from aneurysm or mediastinal tumour
	Foreign body
	Congenital stenosis
Lower œsophageal dysphagia	Achalasia
	Peptic ulcer of œsophagus
	Peptic œsophagitis
	Corrosive œsophagitis
	Simple stricture
	Carcinoma of œsophagus
	Carcinoma of fundus of stomach
	Tertiary contractions with functional diverticula

Grouped into the usual causes at each decade:—

First decade	Congenital atresia or stenosis
	Achalasia
Second decade	Oesophagitis from accidental drinking of a corrosive substance
	Congenital stenosis
	Achalasia
Third decade	Achalasia
Fourth and fifth decade	Syndrome with iron deficiency in women
Fifth, sixth and seventh decade	Peptic ulcer of the œsophagus
	Carcinoma of the œsophagus
	Pharyngocele
	Tertiary contractions with functional diverticula

Simple stricture in children, usually boys, may represent a congenital narrowing, usually about level with the 7th dorsal vertebra. In infancy, vomiting occurs, particularly after the first few mouthfuls, and lumpy food may precipitate an attack. This may be associated with a short œsophagus and partial thoracic stomach. Improvement may follow dilatation. Achalasia is the differential diagnosis of this rare condition in children.

Achalasia.—Although this is most common in the third decade, it may begin during childhood. The condition is almost certainly a neuromuscular defect, causing failure of relaxation of the lower end of the œsophagus. The œsophagus becomes very dilated, and normal peristaltic waves do not occur. A column of fluid at least seven inches high is needed to make fluid pass through into the stomach. The presence of this water-lock prevents the formation of the usual gas-bubble in the fundus of the stomach. The symptoms are, at first, usually intermittent with a sense of fulness, and delay in the passage of food, felt behind the sternum, but the discomfort may

sometimes be referred to the upper part of the œsophagus. Regurgitation of food and fluid without nausea will occur, and loss of weight is common. There is a curious disparity between the severity of the symptoms and the X-ray appearance. A grossly dilated and tortuous œsophagus may be found sometimes with a minimum of symptoms. It has been known for some time that amyl nitrite causes relaxation, but the cardiovascular reaction is too severe to allow its routine use. Field has recently shown that a chemical relation, octyl nitrite, has the same effect on the lower œsophagus, and it may be of great use in the treatment of this distressing condition. A few sniffs from a simple inhaler (B.D.H.) may cause relaxation, and allow the food to pass through into the stomach. This treatment is not always effective, and mercury bougie or operative treatment may be necessary. A good knowledge of the psychological background of the patient is important, as anxiety and difficulties may much aggravate the symptoms.

The syndrome with iron deficiency anæmia.—The so-called Plummer Vinson or Patterson Kelly syndrome consists of an upper dysphagia with the symptoms and signs of anæmia, chiefly in women during the reproductive period of life, and is associated with cracks at the corners of the mouth (cheilosis), glossitis, and hollow, brittle nails (koilonychia). It will respond slowly to iron (fersolate, 3 grains (0.2 gm.) t.d.s.) and an improved diet, but the dysphagia and cheilosis may clear up within a few days if riboflavin, 5 mgm., is given daily by injection. Carcinoma of the post-cricoid region is particularly liable to develop in women who have suffered from this iron deficiency syndrome.

Peptic ulcer of the œsophagus.—This is usually associated with a congenitally short œsophagus. The vertical junction of the œsophagus into the thoracic portion of the stomach allows easy regurgitation of acid gastric juice into the œsophagus. This may cause a peptic œsophagitis or ulceration. It is less uncommon than has been previously thought, and it is invariably misdiagnosed. It must be in the clinician's mind, and a special request given to the radiologist, for it is easily missed unless a special radiological technique is employed. There are recurring attacks of burning pain behind the lower sternum, which may radiate to the back. It is felt while actually eating or drinking. At first, only hard foods, or hot, salty or spiced foods may cause pain, but later everything except milk may cause discomfort. The pain, at first, lasts only a few minutes, and it is at once relieved by alkalis, but later it is more prolonged, and less well relieved. The pain may return one to two hours after meals, particularly if the patient bends down. It is also brought on by lying down during the day, and often wakens the patient at night. Dysphagia develops occasionally from the onset, but more frequently when the pain has been present intermittently for several years.

Severe bouts of pain may occur from the stomach becoming distended with air which cannot escape on account of the associated spasm—the so-called "aerogastrie bloqué". Pain may sometimes radiate to the neck and down the left arm, and be mistaken for coronary ischæmia. Hæmatemesis is an important complication. The essentials of treatment are bland feeds during the day, and elevation of the head of the bed to prevent regurgitation of acid juice into the œsophagus.

A pharyngeal diverticulum develops in a weak area in the posterior pharyngeal wall, particularly in elderly, edentulous men. Unchewed masses of food may start the formation of the pouch, which may attain a considerable size, and displace the œsophagus, causing dysphagia. The sac may fill up with food and fluid, which is regurgitated back into the mouth. Operation may be necessary for relief of the symptoms.

Carcinoma of the œsophagus must be fully excluded in middle-aged and elderly patients with dysphagia. A negative barium swallow must not be accepted as excluding a neoplasm. If symptoms persist, an œsophagoscopy should be performed and a barium meal given, and a request made for special examination of the fundus; a

carcinoma in this position may be present with dysphagia, and may be very difficult to diagnose. It is well worth while striving to achieve early diagnosis in malignant disease of the œsophagus and fundus of the stomach, as the newer operative techniques with transthoracic approach offer some chance of cure.

Tertiary contractions with functional diverticula is an interesting condition, recently described by Templeton. It occurs in elderly men, and there are abnormal contractions of the circular muscle of the lower half of the œsophagus, giving a radiological appearance suggesting multiple diverticula.

Vallecular dysphagia is a term that has been used to describe cases in which the only abnormality found has been a delay in emptying of the valleculæ.

Hysterical dysphagia is a diagnosis which should be made only after the greatest care has been taken to exclude organic disease. Myasthenia gravis and bulbar palsy must be excluded.

The investigation of dysphagia should include a detailed history and examination, a full blood count, Wassermann reaction and barium swallow; œsophagoscopy and barium meal may be necessary.

F. Avery Jones, M.D., F.R.C.P.

ASTHMA

Asthma is primarily due to spasm of the bronchial muscle, and true asthma must be distinguished from certain other causes of paroxysmal hyperpnœa. At times confusion may be caused by an early carcinoma of a bronchus, by pressure of a small thoracic tumour, such as an aneurysm, or by paroxysmal hysterical hyperpnœa (which is usually accompanied by paræsthesiæ in the fingers due to incipient tetany). The paroxysmal hyperpnœa previously known as "cardiac asthma" and "renal asthma" can usually be identified by the symptoms and signs of the coincident cardiac or renal failure.

The *cardinal symptoms of true asthma* are attacks of paroxysmal dyspnœa, accompanied by wheezing in the chest and cough; sooner or later in the attacks there is usually the expectoration of a little mucoid sputum, so that once the tenacious plugs of mucus have been coughed up, there is relief. Physical examination in a long-standing case will show chest deformities, either of the emphysematous type or (when the onset is in childhood) with the keel-shaped prominence of the sternum and falling in of the ribs just above the level of the upper surface of the liver. When seen in or soon after an attack the lungs indicate by the inspiratory and expiratory rhonchi and prolonged expiratory sounds the difficulty the patient has in the expiratory phase of breathing.

Causal factors.—It is doubtful if an attack of asthma ever occurs as a result of a single factor: in any given patient there are always a number of causes lying dormant, and when several of these become operative simultaneously and summate with one another an attack is likely to ensue. The chief of these factors are (1) an allergic diathesis, often inherited and of familial origin; (2) hypersensitivity to foreign protein, which may be inhaled *via* the lungs or ingested *via* the alimentary tract; (3) an emotional basis, especially with suggestion, anxiety, or fatigue; (4) respiratory infections; (5) reflex causes arising especially in the nose, throat, stomach or intestines. When seeking the causes of asthma, it is essential to investigate these factors in turn and to eliminate or diminish the intensity of as many as possible. The allergic diathesis cannot be eliminated, but many persons with allergic susceptibilities do not develop asthma unless other causes become operative: it has been demonstrated that the allergic state is less marked when there is some degree of dehydration, such as is produced by diminishing the alkali reserve of the blood; hence the giving of hydrochloric acid to asthmatic children becomes a logical procedure.

Skin tests.—Hypersensitivity to foreign protein is investigated by inoculating into the skin (either intradermally or by the scratch method) extracts of various proteins

sometimes be referred to the upper part of the œsophagus. Regurgitation of food and fluid without nausea will occur, and loss of weight is common. There is a curious disparity between the severity of the symptoms and the X-ray appearance. A grossly dilated and tortuous œsophagus may be found sometimes with a minimum of symptoms. It has been known for some time that amyl nitrite causes relaxation, but the cardiovascular reaction is too severe to allow its routine use. Field has recently shown that a chemical relation, octyl nitrite, has the same effect on the lower œsophagus, and it may be of great use in the treatment of this distressing condition. A few sniffs from a simple inhaler (B.D.H.) may cause relaxation, and allow the food to pass through into the stomach. This treatment is not always effective, and mercury bougie or operative treatment may be necessary. A good knowledge of the psychological background of the patient is important, as anxiety and difficulties may much aggravate the symptoms.

The syndrome with iron deficiency anæmia.—The so-called Plummer Vinson or Patterson Kelly syndrome consists of an upper dysphagia with the symptoms and signs of anæmia, chiefly in women during the reproductive period of life, and is associated with cracks at the corners of the mouth (cheilosis), glossitis, and hollow, brittle nails (koilonychia). It will respond slowly to iron (fersolate, 3 grains (0.2 gm.) t.d.s.) and an improved diet, but the dysphagia and cheilosis may clear up within a few days if riboflavin, 5 mgm., is given daily by injection. Carcinoma of the post-cricoid region is particularly liable to develop in women who have suffered from this iron deficiency syndrome.

Peptic ulcer of the œsophagus.—This is usually associated with a congenitally short œsophagus. The vertical junction of the œsophagus into the thoracic portion of the stomach allows easy regurgitation of acid gastric juice into the œsophagus. This may cause a peptic œsophagitis or ulceration. It is less uncommon than has been previously thought, and it is invariably misdiagnosed. It must be in the clinician's mind, and a special request given to the radiologist, for it is easily missed unless a special radiological technique is employed. There are recurring attacks of burning pain behind the lower sternum, which may radiate to the back. It is felt while actually eating or drinking. At first, only hard foods, or hot, salty or spiced foods may cause pain, but later everything except milk may cause discomfort. The pain, at first, lasts only a few minutes, and it is at once relieved by alkalis, but later it is more prolonged, and less well relieved. The pain may return one to two hours after meals, particularly if the patient bends down. It is also brought on by lying down during the day, and often wakens the patient at night. Dysphagia develops occasionally from the onset, but more frequently when the pain has been present intermittently for several years.

Severe bouts of pain may occur from the stomach becoming distended with air which cannot escape on account of the associated spasm—the so-called "aerogastrie bloqué". Pain may sometimes radiate to the neck and down the left arm, and be mistaken for coronary ischæmia. Hæmatemesis is an important complication. The essentials of treatment are bland feeds during the day, and elevation of the head of the bed to prevent regurgitation of acid juice into the œsophagus.

A pharyngeal diverticulum develops in a weak area in the posterior pharyngeal wall, particularly in elderly, edentulous men. Unchewed masses of food may start the formation of the pouch, which may attain a considerable size, and displace the œsophagus, causing dysphagia. The sac may fill up with food and fluid, which is regurgitated back into the mouth. Operation may be necessary for relief of the symptoms.

Carcinoma of the œsophagus must be fully excluded in middle-aged and elderly patients with dysphagia. A negative barium swallow must not be accepted as excluding a neoplasm. If symptoms persist, an œsophagoscopy should be performed and a barium meal given, and a request made for special examination of the fundus; a

mentioned, ephedrine, theamin, felsol, riddobron, asthmolysin, and benzyl benzoate are helpful in individual cases. Phenobarbitone or some other form of barbiturate is useful at bedtime, and regular glucose for thin, nervous asthmatic children has proved its worth. Non-specific desensitization is not so commonly used as formerly, as its value is often disappointingly short-lived.

In conclusion, it cannot be too clearly expressed that the successful treatment of asthma lies not so much in the treatment of individual attacks but rather in the treatment of the many facets of the disease, aiming at reducing the intensity of the stimuli which summate and produce attacks, whilst at the same time keeping at as high a pitch as possible the mental and physical health of the subject.

E. C. WARNER, M.D., F.R.C.P.

THE CHOICE OF BARBITURATES

THE various narcotic barbiturates do not differ in any important way in their action on the brain. The effect of any one on the brain is much the same as that of any other, and much the same as the effect of any other of the powerful narcotic drugs, with one exception, morphine. Morphine has many advantages and disadvantages in comparison with other narcotics, and with these in mind the practitioner who is about to prescribe a narcotic should ask himself first of all whether he should try morphine by itself, or morphine in combination with another narcotic, or another narcotic without morphine. Only when he has made his decision on this point should he consider which of the barbiturates he is going to give.

Although the narcotic barbiturates do not differ significantly in their mode of action, they do differ strikingly in the duration of their effect, which depends upon the rate at which their complex molecule is broken down in the body. Upon this different rate of destruction depends the familiar classification of barbiturates. Before discussing this classification it is well to remind the reader that the British Pharmacopœial names of barbiturates end in "—one" and the United States Pharmacopœial names in "—al", and that in many cases delayed official recognition of a widely used drug has had the result that a proprietary name is far more familiar than the official one, for example, pentothal and thiopentone, evipan and hexobarbitone. In some cases a deservedly popular barbiturate is still, after many years, awaiting recognition by the British Pharmacopœia.

CLASSIFICATION

(1) *Long action.*—Barbitone (veronal) and its sodium salt (medinal)
      Phenobarbitone (luminal, gardenal)
      Dial (allobarbitone)
      Soneryl (butobarbitone, neonal)
These differ slightly from each other in their rate of excretion, but all are relatively slowly excreted, and an effective dose leaves the patient a little sleepy next day.

(2) *Short action.*—Amytal
      Pentobarbitone and its sodium·salt (nembutal)
      Seconal
      Cyclobarbitone (phanodorm, phanodorn)
All these are rapidly destroyed in the liver (amytal rather more slowly than the others), and are much less likely to leave the patient sleepy next day.

(3) *Very short action.*—The barbiturates which are used as general anæsthetics, pentothal (thiopentone), evipan (hexobarbitone), and the new compound the trade name of which is "kemithal". The rate of destruction of these drugs is so rapid that they are not suitable for administration as hypnotics.

INDICATIONS

Choice in the treatment of insomnia.—It makes little difference whether a drug in the first or second class be chosen, as the dose usually required to exert a hypnotic

such as are made available by several firms of manufacturing chemists: even so, the results must be interpreted with care and in relation to a careful clinical history of the patient, as otherwise he may be unnecessarily restricted in his food and his everyday life. The fact that positive skin tests by themselves do not prove the cause of asthma is shown by the number of normal people who give positive reactions and yet have never shown symptoms of an allergic disease. Some protein derivatives seem to be of greater importance than others, and feathers, dust, orris root, pollens, fish, and wheat seem to be common offenders: the best proof of any particular foreign protein being of etiological importance is the clinical improvement obtained when it is eliminated. Sometimes it is possible to desensitize a patient by a course of vaccine therapy, but, although in hay fever and hay asthma this can be most helpful, the benefit of vaccinating with other allergens is often short-lived or even disappointing.

Other predisposing factors.—It should be remembered that occasionally drugs may cause allergic outbursts, as can be demonstrated in some people with aspirin. The importance of the psychological factor in causing asthma is well known, and worry, anxiety, overwork, sleeplessness, all play their part. It may or may not be possible to help to combat the many different mental stresses, but there is no question that a well-ordered life, with regular meals, proper sleep and a sufficiency of mental relaxation and adequate holidays can be most important in treatment. Respiratory infections, such as a common cold, or bronchitis, can precipitate most troublesome attacks of asthma; especially in middle and later life an attack of simple bronchitis may induce really severe bronchitic asthma. The bronchial spasm hinders the expectoration of the infected material with consequent increase in the anoxæmic and toxæmic symptoms, and for this reason morphine, even in ordinary doses, can be most dangerous because of its respiratory depressive action.

TREATMENT

Potassium iodide in increasing doses, even up to 30 grains (2 gm.) t.i.d., will sometimes liquefy the sputum sufficiently to enable it to pass through the areas of bronchial spasm; stramonium, hyoscyamus or lobelia may be usefully added as antispasmodics. Chemotherapy with the sulphonamides or with systemic penicillin can be most helpful in combating the infection and, when penicillin-sensitive organisms are present, inhalations of penicillin in vapour form are on trial. Contributory factors producing bronchial spasm by increasing vagus activity can arise from the area of the sensory distribution of the trigeminal nerve, from the stomach or from the intestines: successful treatment of an infected antrum can give a most gratifying relief of asthma, but, on the other hand, radical operative measures to remove hyperæmic middle turbinate bones and nasal spurs are much less favoured now than previously. The avoidance of large and indigestible meals, and of distension of the colon or even the bladder, can be accomplished by commonsense advice.

The drugs which have been used for asthma are legion. For an acute attack, a solution of adrenaline given subcutaneously in doses of 3 to 8 minims (0.18 to 0.5 c.cm.) still remains the best line of treatment, and the earlier in an attack it is given, the more effective it is: sometimes adrenaline in oil is preferred to the usual watery solution, particularly when a longer action is desirable. For status asthmaticus, or for a severe attack, Hurst's method of injecting adrenaline, 1 minim (0.06 c.cm.) subcutaneously each half minute until the attack ceases or until 1 to 3 c.cm. has been given, is still of great value. Intravenous adrenaline has been advocated but may give severe reactions and even prove fatal from ventricular fibrillation. On account of its antispasmodic and sedative effects, intravenous or intramuscular pethidine (50 to 100 mgm.) can be most useful, but its habit-forming propensities must not be forgotten. Sooner or later each asthmatic patient will find which drug and particular method of administration is of most benefit; apart from those already

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Penicillin Lozenges and Sore Tongue

QUERY.—I recently had a patient to whom I gave penicillin throat lozenges (1 two-hourly for six days) for a streptococcal tonsillitis. The tonsillitis settled down at the end of a week but the patient's tongue became swollen and painful as if the superficial layer had peeled off. This healed in one week. The patient was not anæmic. I concluded that the tongue condition was due to the penicillin. Would you kindly advise me on this?

REPLY.—It sometimes happens that after treatment with penicillin lozenges there is an inflammation of the mouth and tongue which passes off when the penicillin treatment is suspended. This does not appear to be due to toxic action of the penicillin but rather to the penicillin functioning too well. Normally there are present in the mouth large numbers of bacteria, and a copious culture of streptococcal types of low virulence can always be obtained. Some of these streptococci are powerful inhibitors of the growth of many other bacteria and they are sensitive to penicillin. When penicillin lozenges are sucked the streptococci disappear, and some of the other bacteria insensitive to penicillin can grow out much more readily than before, as the streptococcal inhibition is removed. In a few patients this disturbance of the normal bacterial balance in the mouth results in an inflammation of varying intensity but fortunately it seems to be only in a few. The obvious treatment is to stop the penicillin while the pathological condition gradually subsides.

SIR ALEXANDER FLEMING, F.R.C.P., F.R.C.S., F.R.S.

Adult Whole Blood in Measles Prophylaxis

QUERY.—In "Revision Corner" in the April number, Dr. Powell Phillips mentions serum for the passive immunization of measles contacts, but says nothing of adult whole blood. An injection of whole blood taken from either parent is a risk, although a most practical method for the general practitioner to adopt. Would it be possible to obtain Dr. Powell Phillips's opinion on this, on dosage, and whether any of the substances suggested carry the risk of encephalitis?

REPLY.—I agree that the giving of adult whole blood would be a practical method for use in general practice, especially as the blood of either parent would probably be available. I have not recommended its use for the following reasons:—

(1) The dose of whole blood has to be double the amount of adult serum. Thus, it would entail a dosage of at least 20 c.cm. for a child under three years, and would have to be increased appropriately for a child over that age. This large bulk carries the risk of a slowly absorbing hæmatoma, with possibility of infection, which cannot be disregarded.

(2) From the immunological point of view, I regard the procedure as rather a "hit or miss method", because it is known that everyone, even though they may have had a previous attack of measles, does not possess the same power to form antibodies. With a pooled serum there is mixed sera from several individuals so that the antiviral antibodies are probably present in an average amount in the mixed adult serum.

(3) The transmission of blood-borne disease cannot be disregarded and the Rh factor cannot be ignored, especially in female children.

With regard to the risk of encephalitis, it is not considered that this complication is in any way liable to occur and this would not be a deterrent to the administration of whole blood.

W. POWELL PHILLIPS, M.R.C.S., L.R.C.P., D.P.H.

Flies, Food and D.D.T.

QUERY.—I should be grateful for any suggestions that you could give me for dealing with a plague of flies and wasps which invades every summer the jam factory to which I am Medical Officer. Would I be justified in using D.D.T. sprays, or is this contraindicated in view of the risk of the jam becoming contaminated?

REPLY (from an industrial chemist).—With regard to flies, it would certainly be undesirable to spray D.D.T. freely where it may come into contact with food; moreover, of course, the usual care should be taken to avoid prolonged contact with the skin. If D.D.T. is sprayed on the walls, say at night, this treatment might be effective. The best way to apply D.D.T. would be to have sprayed surfaces placed in the positions where flies are most common; for example, sprayed panels of wood or something of that kind. There is now on the market a varnish preparation which can be applied over paint work, and which does not affect the appearance of the paint. This

effect on a willing patient is so small that the patient is rarely very sleepy next day, even when a long-action drug is chosen.

Choice in the treatment of epilepsy.—As a suppressive of epileptic attacks the widely used phenobarbitone should certainly be the first choice. The non-narcotic barbiturate, phemitone (prominal or rutonal), may be used instead of phenobarbitone or with it for patients who tend to become drowsy on the effective dose of phenobarbitone. If barbiturates do not completely suppress attacks, sodium diphenyl hydantoinate (soluble phenytoin, epanutin, dilantin) should be used as a supplementary treatment, although the risk of serious toxic effects should be remembered.

When epileptic attacks are chiefly nocturnal a supplementary bedtime dose of a short-action barbiturate is often of value. When attacks are cyclical the dose of the anticonvulsant should be increased just before the danger period, and decreased again when it is past.

In *petit mal* or pyknolepsy results from anticonvulsant therapy are often disappointing; it is important to remember this so as to avoid pressing drugs to the point of dangerous overdosage. Possibly the new hydantoinate, tridione (not yet on the market), will fulfil its promises of success in the prevention of frequent minor attacks.

Choice in checking convulsions.—In conditions such as strychnine poisoning and status epilepticus the injectable barbiturate most likely to be at hand is sodium pentothal, and it should be given. Its effect, however, wears off quickly, and the injection may have to be repeated frequently, for which reason sodium amytal or sodium pentobarbitone (nembutal) is a better choice. It should be noted that in strychnine poisoning the dose must be high, and that, as death is probably imminent without treatment, it is wiser to err on the side of overdosage. In status epilepticus, on the other hand, a small dose is often effective, and the gravity of the condition does not justify the single administration of a single dangerously large dose.

In convulsive states it is often impossible to keep the patient quiet enough to allow a vein to be injected; in such cases the injection should be given into a muscle.

Choice in the treatment of delirium.—The most common mistake in the treatment of delirium is to neglect morphine and to rely on a barbiturate. In many types of delirium (in nearly all types associated with pain or fever) morphine should be tried first. If the physician is afraid of morphine he can begin with a small dose and stand by to repeat it in twenty minutes; he will usually find that each repeated dose quietens the patient more and more without producing a significantly deeper level of narcosis.

With a barbiturate, on the other hand, it may prove impossible to calm a delirious patient without depressing him to the stage of surgical anæsthesia, and if the drug be given by fractional administration the first effect of a small dose is often to make the delirium more violent and uncontrolled, with the result that too much drug is given and dangerously profound narcosis produced.

Sodium luminal (sodium phenobarbitone) is emphatically not the right barbiturate to administer in delirium. It was once widely recommended, but only because it was at that time the only injectable barbiturate. In those rare cases of delirium in which morphine produces no calming effect the best treatment is intravenous sodium pentothal, administered slowly until the signs of the first plane of third-stage anæsthesia appear. In effect, the problem of treating delirium is little different from that of securing a quiet second-stage anæsthesia, and a very good reason for relying upon morphine and pentothal is that they are drugs with which the modern practitioner is familiar.

Why barbiturates fail.—It should never be forgotten that a barbiturate administered orally may fail to act simply because it has not been absorbed. The tablet if swallowed uncrushed may not dissolve, or the capsule may not have yielded up its contents.

R. H. MICKS, M.D., F.R.C.P.I.

of the combination four-hourly until defervescence and other clinical signs indicated significant improvement, when the dose was reduced to 1 gm. six-hourly. The response to treatment was rapid and satisfactory, and in only one case were any toxic signs or symptoms encountered—in this instance drug fever. No attempt was made to give large amounts of fluid, and alkalis were not administered. A satisfactory blood concentration of sulphonamide was attained in all cases. Of more than 300 specimens of urine examined, only 21 were found to contain any crystals; these were never excessive and were usually of the sulphathiazole type. The significance of this last observation can be assessed from the fact that other observers have noted an incidence of 29 per cent. of urinary crystals in patients treated with sulphadiazine, and of 70 per cent. in patients treated with sulphathiazole. One explanation advanced for the low incidence of allergic reactions is that the duration of treatment with the combination of sulphathiazole and sulphadiazine was shorter than that usually required with either preparation alone, and that this meant that treatment was discontinued before hypersensitivity to the drug developed.

Benzedrine in the Treatment of Acute Barbiturate Poisoning

THE dangers inherent in the use of picrotoxin led A. W. Freireich and J. W. Landsberg (*Journal of the American Medical Association*, June 22, 1946, **131**, 661) to investigate the effect of amphetamine sulphate (benzedrine) in acute barbiturate poisoning. The original dosage used was 10 mgm. of amphetamine sulphate dissolved in 1 c.cm. of isotonic solution of sodium chloride, given intravenously without dilution. Later it was found that the dosage could be raised to an initial dose of 40 mgm. of the undiluted drug, followed by 20 mgm. every thirty minutes. In addition, the usual supportive treatment was given, such as fluids intravenously. Notes are supplied of fourteen patients to whom this treatment was given; all recovered except one, and in this case the failure to respond to treatment is attributed to inadequate dosage due to supplies of the drug running out. No toxic effects except headache were observed, in spite of the fact that large amounts were often required; in one case, for instance, 400 mgm. of amphetamine were given intravenously. One of the patients had hyperthyroidism, and this was not adversely affected by the treatment. Stress is laid upon the fact that it is essential in all cases of barbiturate poisoning, no matter how mild they may appear to be, to institute treatment as quickly as possible.

Percorten as a Post-Operative Peristaltic Stimulant

PERCORTEN, a synthetic suprarenal hormone (1 per cent. desoxycorticosterone-glucoside solution) has been used as a post-operative peristaltic stimulant in a series of fifty cases of intra-abdominal operations. The results are recorded by W. Stähli (*Schweizerische Medizinische Wochenschrift*, June 6, 1946, **76**, 609). The drug is supplied in 5 c.cm. ampoules of 50 mgm. desoxycorticosterone-glucoside (Ciba), and the procedure adopted was as follows:— On the first post-operative evening an intravenous injection of 50 mgm. was given; on the first and second post-operative days three injections of 1 ampoule (50 mgm.) were given, and on the third post-operative day two injections of 1 ampoule. If no severe peristaltic disturbance was present, only 2 ampoules were administered on the first and second post-operative days. The maximum daily total dose employed was 150 mgm. and the maximum total dose for the post-operative course was 500 mgm. No secondary reactions of importance or signs of intolerance were noted, apart from slight symptoms of hypoglycæmia in patients who for some time before operation had been unable to take sufficient nourishment; these symptoms quickly subsided after injections of dextrose. In twenty-one of the fifty patients a beginning of intestinal function was noted on the evening of the first post-operative day, and in twenty-four during the course of the second post-operative day. In two cases of paralytic ileus, injections of percorten did not suffice for the stimulation of peristalsis and also in two cases in which cholecystectomy had been performed. In all the treated cases there was a markedly favourable action on the general condition, and particularly on the peripheral circulation. The incidence of post-operative shock was low and the patients had shortened and mild convalescent courses.

Volatile Oils as Expectorants

USING their standardized technique of measuring the respiratory tract fluid (R.T.F.), E. M. Boyd and G. L. Pearson (*American Journal of Medical Sciences*, May 1946, **211**, 602) have investigated in the experimental animal the expectorant properties of a series of volatile oils. The most effective was found to be *Oleum anisi* (oil of aniseed) which increased the rate of output of R.T.F. as much as sixfold. *Oleum terebinthinæ* (oil of turpentine) also produced a definite increase in R.T.F., but *Terebenum* and *Terpini hydras* had relatively little effect. *Oleum abietis* (oil of Siberian fir) was almost as potent as oil of turpentine. *Oleum limonis* and

varnish preparation is made by Docker Brothers, Ladywood, Birmingham, 16, and is marketed by them under the name of "Hermaddite AF 34". I would advise your subscriber to write to them asking for their pamphlet which describes the application of this varnish on what are called the "hot spots" of the room. Of course, the most satisfactory remedy is to trace, if possible, where the flies come from. Obviously they should not be breeding in the factory, and if the spaces outside are under the control of the factory it might be possible to keep the premises clear of flies.

Wasps.—I am afraid that on this matter I can give you no advice. So far as I know, the only effective remedy is to fix gauze or wire-mesh protection over the window spaces.

Post-Diphtheritic Polyneuritis

QUERY.—I have a patient, a girl aged seventeen, recently discharged from an isolation hospital following an attack of diphtheria. There is weakness most marked in the left leg and both knee-jerks are absent. Can you suggest any treatment?

REPLY.—No special treatment is indicated as complete recovery will almost certainly occur within two to three months. Care should be taken to avoid overstretching the weakened muscles. Contractures and permanent paralysis are unknown in post-diphtheritic polyneuritis, although they can follow the very rare myelopathy of vascular origin which occurs in this infection. Vitamin B_1—an alleged panacea in all forms of neuritis—does not expedite recovery; massage and electricity are unnecessary, although voluntary movements should be encouraged.

PROFESSOR HENRY COHEN, M.D., F.R.C.P.

The Treatment of Rheumatoid Arthritis

QUERY.—I shall be grateful for suggestions as to the best method of treating a man aged fifty-six who has had generalized rheumatoid arthritis for about three years. He has a pulse rate of up to 110 when not at rest in bed; normal in bed. His temperature is not raised.

The pain is very severe, especially in shoulders and spinal joints. He has had so gold injections but the reaction was so sev that it had to be discontinued. He has also h calcium iodide or osteocalcium, has been hospital for lengthy periods and undergone course of massage. Sulphonamides have be tried. His limbs are capable of being painles moved passively nearly to a full range, b there is a tendency to crepitation in one wri The wrists are markedly swollen. What are tl conditions indicating rest or movements acti or passive in such a case? Would balneotherap be worth recommending? Could pethidine k administered as an analgesic without risk over prolonged period as the ordinary analgesics c the "empirin" type seem ineffective to a larg degree?

REPLY.—It would appear that the disease is i an active phase. The basic principles of treat ment for each affected joint are:—Rest in th optimum position; the minimum of weigh bearing; daily passive movements by a physio therapist; frequent active exercises to counter act the muscle wasting. A plaster "shell" woul be of benefit to the spine, whilst X-ray irradia tion may (dramatically at times) relieve the pain in the back. Plaster "cock-up" splints for the wrists are indicated. There is a view that the heart is not infrequently involved in rheuma toid arthritis, but as the patient has had the disease for three years and is fifty-six years of age, there may be some other factor to account for the tachycardia; it would be unwise to assume that a rheumatic carditis is present. It is likely that the erythrocyte sedimentation rate is markedly increased and that there is a severe hypochromic anæmia. In spite of the fact that reactions to gold have previously occurred, it is probable that a course of Crookes' calcium gold (said to be less toxic than the sodium salt), in dosage of 25 mgm. weekly, would prove a useful adjuvant. For the anæmia, iron and ammonium citrate, 30 grains t.d.s., should be prescribed. Balneotherapy at a spa such as Bath, Buxton or Droitwich would help at a later stage to overcome muscle spasm and wasting. Pethidine is much inferior in rheumatoid arthritis to aspirin plus codeine, which should be freely given.

PRACTICAL NOTES

Sulphonamide Mixtures

As a means of reducing the incidence of renal complications, D. Lehr (*Journal of Urology*, May 1946, **55**, 564) recommends the use of a mixture of equal parts of sulphathiazole and sulphadiazine. His conclusions are based upon a series of 70 patients with acute bacterial infections, including 26 cases of pneumonia, 11 cases of bronchitis, 14 cases of tonsillitis and 6 cases of otitis media. The dosage used was an initial dose of 4 gm. (2 gm. of sulphathiazole and 2 gm. of sulphadiazine), followed by 2 gm.

to pH 7.4. This solution was applied to the lesion with a large swab every two hours during the day, and in addition the entire mouth was swabbed with the solution thrice daily. In one severe case the lesion had completely disappeared after twenty days' treatment, whilst in the other five, less severe, cases, the lesions disappeared after four to ten days' treatment. He also reports satisfactory results in one adult with extensive cutaneous moniliasis, in whom the vagina was also involved. In this patient, for the cutaneous lesion, the following ointment was used:—

Caprylic acid	..	..	10.0
Diethylene glycol monoethyl ether			3.0
Carbowax (6000)	..	..	47.5
n-propyl alcohol	..	..	10.0
Zinc caprylate	..	..	5.0
Sodium hydroxide	..	..	2.45
Water	..	..	22.05

Enough sodium hydroxide is added to adjust to pH 8.0.

For the vaginal infection the following jelly was used:—

Caprylic acid	..	..	10.0
Glycerin	..	..	10.0
Gum tragacanth	..	..	12.0
Gum acacia	..	..	9.0
Water	..	..(approx.)	55.0

Enough sodium hydroxide is added to adjust to pH 6.75.

The response to this jelly was excellent, but it caused considerable irritation for thirty minutes after instillation. It was therefore replaced with a 10 per cent. sodium caprylate talcum powder mixture which was blown into the vagina thrice weekly. This also caused some irritation, but less than the jelly.

The Treatment of Prostatic Carcinoma

IN an article on the treatment of prostatic carcinoma with hormones, G. Reimann-Hunziker (*Praxis*, July 11, 1946, **35**, 449) says that only radical operation can give hope of complete cure. Castration and œstrogenic therapy, however, can prolong life and in many cases can procure a temporary disappearance of the pain and dysuria. A combination of castration followed by transurethral electroresection and prolonged stilbœstrol medication results in the best survival rate. The improvement is only temporary, and on an average lasts for six or more months. The hope that retrogression of the growth would render it operable has not been confirmed. Determination of the serum phosphatase is of use in prognosis and for estimation of the effects of treatment; a high phosphatase ratio is always suggestive of bone metastases. Oestradiol dipropionate, diethylstilbœstrol dipropionate and diacetate are suitable preparations for oral or parenteral use; recently implantation of tablets or crystals has been used. The dosage depends upon the individual case; the usual dosage employed at the Surgical Clinic of Basle University is 1 mgm.

stilbœstrol daily up to a total dose of 50 mgm. The results are often surprising—disappearance of the pain and disturbances of micturition, improvement in the general condition, increase in weight, and retrogression of the primary growth and metastases. Secondary reactions in the form of changes in the breast and œdema of the legs, penis and scrotum may occur.

Shortage of Bismuth

IN an editorial note in *The Pharmaceutical Journal* (July 13, 1946, **157**, 18) attention is drawn to the fact that bismuth salts are still in short supply due to the small quota of the metal manufacturers are receiving. The shortage has been accentuated by an eight-months' strike in the smelting industry in U.S.A., which has only recently terminated. This means that at least three months will elapse before manufacturers will again be able to fulfil orders completely. In order to conserve supplies it is therefore essential that practitioners should continue to prescribe bismuth only for the treatment of syphilis and tropical diseases, as recommended in the National War Formulary (N.W.F.). In place of mixtures, powders and lozenges containing bismuth the N.W.F. gives the following alternatives:—

Mistura Kaolini
Mistura Kaolini et Morphinæ
Mistura Magnesii Carbonatis
Mistura Magnesii Carbonatis Aromatica
Pulvis Kaolini Compositus
Pulvis Magnesii Trisilicatis Compositus
Tabella Magnesii Carbonatis Composita
Mistura Calcii Carbonatis Composita pro Infantibus

Trichoptilosis

IN an article dealing with different affections of the scalp, L. Gallerand and E. Juster (*Presse Médicale*, July 6, 1946, **54**, 449) devote a section to trichoptilosis and its treatment. Trichoptilosis is characterized by two symptoms, i.e. splitting of the ends and fragility of the hairs, which break easily on pulling. The condition is due principally to bad quality soaps and shampoos. The treatment consists in greasing the ends of the hair every day, either with a brush or a spray. The chief difficulty is to find a good brilliantine for the purpose. The following are recommended by the authors:—

(1) Castor oil	..	..	20 gm.
Ox marrow	..	..	12 gm.
(2) Castor oil	..	..	10 c.cm.
Liquid paraffin	..	..	10 c.cm.
Essence of cedar	..	..	10 c.cm.
Essence of violet	..	..	3 c.cm.
(3) Castor oil	..	..	100 c.cm.
Alcoholate of lavender	..	100 c.cm.

Another section deals with follicular lesions of the scalp in men due to the use of brilliantines or darkening oils of bad or impure quality. The lesions resemble those seen in workers who handle impure oils during their employment.

Oleum eucalypti both produced considerable increase in the output of R.T.F. *Tinctum benzoini composita* (Friar's balsam), on the other hand, had little effect. The mode of action of these volatile oils as expectorants is not clear, but it is probably not a reflex action from the stomach, as section of the afferent gastric nerves had little effect upon their expectorant action. The suggestion is made that they may stimulate directly the secretory cells of the respiratory tract. Confirmation is thus provided for the constituents of many of the old-established expectorant mixtures.

Benadryl in the Treatment of Allergic Conditions

PRELIMINARY reports from the U.S.A. suggest that benadryl (β-dimethylaminœthyl benzhydril ether hydrochloride) is an effective drug in the treatment of certain allergic conditions. G. L. Waldbott (*Journal of Allergy*, May 1946, **17**, 142) has investigated its action in 165 patients. The most satisfactory results were obtained in urticaria: 16 out of 20 patients reported prompt and marked relief lasting for as long as four hours after taking a capsule containing 50 mgm. of the drug. In the majority of these the symptoms tended to recur after four to six hours, but were relieved by a second capsule. Of 31 patients with hay fever, only eight failed to show at least some improvement. The results in asthma were not so satisfactory: of 48 patients with "perennial" asthma, 24 showed no improvement, while of 30 with "seasonal" asthma, 16 failed to respond. The majority of the patients complained of slight toxic effects; of the 165 patients, only 73 had no side-effects from the drug, 81 complained of dizziness and drowsiness, four of nausea, two of muscular twitching, one of paræsthesiæ, and one of vomiting. In three instances administration of the drug was followed by asthmatic attacks. Comparable results are reported by S. J. Levin (*Ibid.*, May 1946, **17**, 145) in a series of 223 patients. The usual dosage in adults was 50 to 100 mgm. every four to six hours. Sixty per cent. of the entire series was relieved by the drug, the figures for the various subgroups being: 72 cases of asthma, 47 (65 per cent.) relieved; 68 cases of hay fever, 40 (58 per cent.) relieved; nine cases of urticaria, six (60 per cent.) relieved; 15 cases of migraine, nine (60 per cent.) relieved. The number of reactions was high (144 cases), drowsiness being the most frequent complaint. In four cases of asthma the condition was aggravated by the drug. Of 83 patients with hay fever, bronchial asthma, or both these conditions, G. A. Koelsche *et al.* (*Ibid.*, May 1946 **17**, 151) report that 69 per cent. responded well to benadryl in doses of 50 to 100 mgm. thrice daily. The results in hay fever were much better than those in asthma: 75 per cent. of 52 patients with hay fever obtaining relief, compared with only 33 per cent. of 12 patients with asthma.

Penicillin in the Treatment of Agranulocytosis

THE successful treatment of a case of severe agranulocytosis resulting from chrysotherapy and complicated by rapidly progressive folliculitis and marked toxæmia is recorded by E. W. Boland, N. E. Headley and P. S. Hench (*Proceedings of the Staff Meetings of the Mayo Clinic*, May 15, 1946, **21**, 197). The patient, an officer aged thirty-nine, was treated for severe progressive rheumatoid arthritis by intramuscular injections of gold, in dosage of 25 mgm. weekly for three weeks and thereafter 50 mgm. weekly. Just over two months after the institution of treatment the patient developed headache and malaise and a number of boils were present in the axillæ and inguinal region which by the evening of the same day had spread to other parts of the body. He was admitted to hospital with a temperature of 102° F. (38.9° C.). The total leucocyte count was 3,400 and no neutrophils were present. Penicillin, in dosage of 40,000 units three-hourly, by intramuscular injection, up to four injections and then 20,000 units three-hourly day and night was given, with pentose nucleotide, yellow bone marrow and a blood transfusion. On the fourth day of the acute illness there was a remarkable and dramatic improvement; the headache had disappeared, the pharynx appeared normal, the temperature had dropped to 100° F. (37.8° C.), and the leucocyte count was 4,100, with neutrophils 20 per cent. The following day the patient was afebrile, the skin lesions were rapidly subsiding, and the leucocyte count was 5,200, neutrophils 44 per cent. Four days after the institution of penicillin therapy the patient was ambulant with a normal blood picture. The total amount of penicillin administered was 880,000 units in five days.

Sodium Caprylate in the Treatment of Thrush

POINTING out how unsatisfactory is the present treatment of moniliasis of the skin and mucous membrane, E. L. Keeney (*Bulletin of the Johns Hopkins Hospital*, June 1946, **78**, 333) recommends the use of sodium caprylate. In six patients, all infants or young children, he obtained excellent results with a 20 per cent. aqueous solution of sodium caprylate adjusted

to pH 7.4. This solution was applied to the lesion with a large swab every two hours during the day, and in addition the entire mouth was swabbed with the solution thrice daily. In one severe case the lesion had completely disappeared after twenty days' treatment, whilst in the other five, less severe, cases, the lesions disappeared after four to ten days' treatment. He also reports satisfactory results in one adult with extensive cutaneous moniliasis, in whom the vagina was also involved. In this patient, for the cutaneous lesion, the following ointment was used:—

Caprylic acid	..	..	10.0
Diethylene glycol monoethyl ether			3.0
Carbowax (6000)	..	..	47.5
n-propyl alcohol	..	..	10.0
Zinc caprylate	..	..	5.0
Sodium hydroxide	..	..	2.45
Water	..	..	22.05

Enough sodium hydroxide is added to adjust to pH 8.0.

For the vaginal infection the following jelly was used:—

Caprylic acid	..	..	10.0
Glycerin	..	..	10.0
Gum tragacanth	..	..	12.0
Gum acacia	..	..	9.0
Water	..	..(approx.)	55.0

Enough sodium hydroxide is added to adjust to pH 6.75.

The response to this jelly was excellent, but it caused considerable irritation for thirty minutes after instillation. It was therefore replaced with a 10 per cent. sodium caprylate talcum powder mixture which was blown into the vagina thrice weekly. This also caused some irritation, but less than the jelly.

The Treatment of Prostatic Carcinoma

IN an article on the treatment of prostatic carcinoma with hormones, G. Reimann-Hunziker (*Praxis*, July 11, 1946, **35**, 449) says that only radical operation can give hope of complete cure. Castration and œstrogenic therapy, however, can prolong life and in many cases can procure a temporary disappearance of the pain and dysuria. A combination of castration followed by transurethral electroresection and prolonged stilbœstrol medication results in the best survival rate. The improvement is only temporary, and on an average lasts for six or more months. The hope that retrogression of the growth would render it operable has not been confirmed. Determination of the serum phosphatase is of use in prognosis and for estimation of the effects of treatment; a high phosphatase ratio is always suggestive of bone metastases. Oestradiol dipropionate, diethyl-stilbœstrol dipropionate and diacetate are suitable preparations for oral or parenteral use; recently implantation of tablets or crystals has been used. The dosage depends upon the individual case; the usual dosage employed at the Surgical Clinic of Basle University is 1 mgm.

stilbœstrol daily up to a total dose of 50 mgm. The results are often surprising—disappearance of the pain and disturbances of micturition, improvement in the general condition, increase in weight, and retrogression of the primary growth and metastases. Secondary reactions in the form of changes in the breast and œdema of the legs, penis and scrotum may occur.

Shortage of Bismuth

IN an editorial note in *The Pharmaceutical Journal* (July 13, 1946, **157**, 18) attention is drawn to the fact that bismuth salts are still in short supply due to the small quota of the metal manufacturers are receiving. The shortage has been accentuated by an eight-months' strike in the smelting industry in U.S.A., which has only recently terminated. This means that at least three months will elapse before manufacturers will again be able to fulfil orders completely. In order to conserve supplies it is therefore essential that practitioners should continue to prescribe bismuth only for the treatment of syphilis and tropical diseases, as recommended in the National War Formulary (N.W.F.). In place of mixtures, powders and lozenges containing bismuth the N.W.F. gives the following alternatives:—

Pulvis Kaolini Compositus . Aromatica
Pulvis Magnesii Trisilicatis Compositus
Tabella Magnesii Carbonatis Composita
Mistura Calcii Carbonatis Composita pro Infanibus

Trichoptilosis

IN an article dealing with different affections of the scalp, L. Gallerand and E. Juster (*Presse Médicale*, July 6, 1946, **54**, 449) devote a section to trichoptilosis and its treatment. Trichoptilosis is characterized by two symptoms, i.e. splitting of the ends and fragility of the hairs, which break easily on pulling. The condition is due principally to bad quality soaps and shampoos. The treatment consists in greasing the ends of the hair every day, either with a brush or a spray. The chief difficulty is to find a good brilliantine for the purpose. The following are recommended by the authors:—

(1) Castor oil	..	..	20 gm.
Ox marrow		..	12 gm.
(2) Castor oil	..	..	10 c.cm.
Liquid paraffin	..	..	10 c.cm.
Essence of cedar	..	..	10 c.cm.
Essence of violet	..	..	3 c.cm.
(3) Castor oil	..	..	100 c.cm.
Alcoholate of lavender	..	100 c.cm.

Another section deals with follicular lesions of the scalp in men due to the use of brilliantines or darkening oils of bad or impure quality. The lesions resemble those seen in workers who handle impure oils during their employment.

REVIEWS OF BOOKS

Penicillin. Its Practical Application. Under the general editorship of PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S. London : Butterworth & Co. (Publishers), Ltd., 1946. Pp. 380. Figures 59. Price 30s.

As is only meet, this, the first textbook on the subject to be published in this country, appears under the skilled editorship of Sir Alexander Fleming. Essentially practical in its outlook, it is assured of a warm welcome as a mine of authoritative information essential to every practising doctor, whether physician or surgeon, general practitioner or specialist. The editor has collected a team of distinguished contributors, all of whom have personal experience of the use of penicillin. A preliminary section is devoted to chapters dealing with some of the general aspects, such as the chemistry and manufacture, the pharmacy, the pharmacology, and methods of administration. In addition it includes two chapters by the editor himself: one on the history and development of penicillin, and the other on bacteriological control of penicillin therapy. The greater part of the book is devoted to the clinical use of penicillin and covers the subject in great detail. Successive chapters deal with its use in generalized infections, bacterial endocarditis, chest infections, chest surgery, wounds and gas-gangrene, burns and plastic surgery, orthopædic surgery, hand infections, osteomyelitis, abdominal infections, obstetrics and gynæcology, sepsis neonatorum, brain and meningeal infections, venereal diseases, ophthalmology, otorhinolaryngology, dermatology, and dental and oral infections. There is also a chapter on "penicillin in animal diseases". The concluding chapter is entitled "penicillin and the general practitioner". In spite of the rapidity with which new information concerning penicillin is appearing, the work is well up to date. The wheel of destiny has indeed turned full circle since the medical profession failed to appreciate the significance of the now historic article in which Fleming reported in 1929 his discovery of penicillin. In that article the author, with prophetic foresight, remarked: "it may be an efficient antiseptic for application to, or injection into areas infected with penicillin-sensitive microbes". As the fulfilment of this prophecy, this volume will take a high place in the annals of medical literature.

The Causation of Appendicitis. BY A. RENDLE SHORT, M.D., B.S., F.R.C.S. Bristol: John Wright & Sons, Ltd. Pp. viii and 79. Price 10s.

THE author has long been interested in the search for the cause of appendicitis. He reviewed the subject in the *British Journal of Surgery* in 1920, and in this book he presents the same thesis with much added material. He starts with the marked increase in appendicitis that took place between 1895 and 1905. That the disease was rare in the preceding century is known but, as the author points out, it cannot be assumed that it was equally rare in Tudor and Stuart times. He concludes that King Stephen died of appendicitis, but in stating that no other King of England seems to have been a victim of the disease he forgets the illness and operation of King Edward VII on the eve of his coronation, events that were responsible for a boom in fashionable appendicitis and for two famous lines by the poet laureate of the day:—

"Along the wires the electric message came,
He is not better, he is much the same."

The book bears evidence of years of careful research, and is a storehouse of useful information not easily found elsewhere. The incidence of appendicitis at different periods in different countries and in different racial stocks is studied and reviewed in its relation to social and economic factors, and the many changes in diet that have occurred simultaneously. All these factors are susceptible of several interpretations, and the diagnosis of "appendicitis" alone means something very different in different countries and at different times. "Appendicitis" is the refuge of the diagnostically destitute, the stock-in-trade of the commercial, and the repute and integrity of any surgeon stands roughly in inverse proportion to that of appendicectomy in his practice. The difficulty of coming to any conclusion is shown by the figures from the Falkland Islands, where there were forty operations in 1936, twenty-two in 1937, five in 1938; as the author points out these figures might be attributed to the recent formation of a nutrition board, to the lack of any further appendices to remove, or to a change of surgeon. On the next page he points out that the national distribution of appendicitis varies with the degree of civilization; the Falkland Islands have a long lead, and the United States come second!

The author, whilst keeping an open mind, inclines to the view that a lack of cellulose in the diet is the chief factor responsible for the rise in appendicitis during the years under review, and that a temporary return to rough food accounted for the drop noted in many countries during the two world wars. This is a fascinating book on a difficult subject.

101 *Clinical Demonstrations to Nurses.* By HAMILTON BAILEY, F.R.C.S. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. 136. Figures 138. Price 10s. 6d.

THIS book, primarily intended for nurses, contains much that is of value to practitioners, students and surgeons. As may be expected from this combination of author and publisher, it is beautifully produced and the illustrations, which are the backbone of the book, are superb. Mr. Hamilton Bailey clearly recognizes the importance of the visual memory, a hundred and one clinical abnormalities are depicted, and the illustrations of these are amplified by a short description in anectodal or chatty style, as if the reader were standing with the author at the bedside. Some of the pictures are clinical demonstrations in themselves. Where such excellence abounds it would be captious to be unduly critical, but it must be admitted that Mr. Hamilton Bailey's sense of the dramatic prompts him at times to include illustrations of rarities—for example, Madame Dimanche's now famous sebaceous horn—or extreme examples of common conditions, for instance, the extensive keloid and monstrous meningocele. Nevertheless, if nurses and practitioners are unlikely ever to encounter such conditions, their representation heightens the interest and they are clearly remembered. In the description of dermoid cysts, the distinction between the sequestration dermoid, such as is shown here at the outer canthus, and the ovarian teratomatous dermoid, is not clearly drawn, so that the reader is misled into expecting hair and teeth in the former as well as the latter! The Ochsner-Sherren treatment of appendicitis is not the watchful care of a formed appendix abscess, as is here suggested, and the author might find himself at variance with the majority of surgeons in regard to the pathology of perinephric abscess. But these are unimportant details. Practitioners as well as nurses and students are advised to get the book and to capture or recapture the thrill of clinical surgery as expounded by Mr. Hamilton Bailey, whose publications have always been redolent of the bedside and have so exemplified the special genius of British teaching.

Occupational Therapy for the Limbless. By PHYLLIS LYTTLETON, C.S.P., M.A.O.T. London: H. K. Lewis & Co. Ltd., 1946. Pp. 40. Figures 12. Price 3s.

THE stage between loss of a limb and the provision of a substitute is difficult. This book will help, not only occupational therapists, for whom it is written, but also medical practitioners and others concerned with assisting the patient's powers of adaptation. A wise psychological approach is rightly stressed and some pitfalls are indicated. Detailed examples are given of the promotion, by various crafts, of function in the remaining member and the stump of its fellow. Naturally the upper limb demands much fuller consideration than the lower. Double amputations, which present especially difficult problems, receive attention.

NEW EDITIONS

Antenatal and Postnatal Care, by FRANCIS J. BROWNE, M.D., D.SC., F.R.C.S.ED., F.R.C.O.G., in its sixth edition (J. & A. Churchill Ltd., 25s.) has been revised throughout. New information on erythroblastosis fœtalis and the Rh factor, placenta prævia, toxæmias of late pregnancy and venereal disease in pregnancy has been included, and new sections added on acroparæsthesia, angular pregnancy, and the effect of rubella and other infectious diseases during pregnancy on the causation of congenital abnormalities. The new edition is well illustrated, containing, in all, 90 figures.

OWING to the breakdown of the German publishing organizations the tenth edition of Emil Villiger's *Die Periphere Innervation,* edited by Professor Eugen Ludwig of Basle University, has been produced by Benno Schwabe & Co. of Basle (Sw. frs. 16). The new edition of this well-known textbook on the anatomy of the peripheral nervous system and its essential connexion with successful treatment, is a beautiful production, and congratulations are due both to the editor and to the publishers.

CONSIDERABLE additions have been made to the bibliography in the preparation of the third edition of *Sternal Puncture,* by A. PINEY, M.D., M.R.C.P., and J. L. HAMILTON-PATERSON, M.D., M.R.C.S. (William Heinemann (Medical Books) Ltd., 15s.). That a third edition has been called for so soon after the appearance of its predecessor is testimony to the value of this work and the demand for more information on a procedure which is of growing importance in diagnosis.

REVIEWS OF BOOKS

Penicillin. Its Practical Application. Under the general editorship of PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S. London : Butterworth & Co. (Publishers), Ltd., 1946. Pp. 380. Figures 59. Price 30*s.*

As is only meet, this, the first textbook on the subject to be published in this country, appears under the skilled editorship of Sir Alexander Fleming. Essentially practical in its outlook, it is assured of a warm welcome as a mine of authoritative information essential to every practising doctor, whether physician or surgeon, general practitioner or specialist. The editor has collected a team of distinguished contributors, all of whom have personal experience of the use of penicillin. A preliminary section is devoted to chapters dealing with some of the general aspects, such as the chemistry and manufacture, the pharmacy, the pharmacology, and methods of administration. In addition it includes two chapters by the editor himself: one on the history and development of penicillin, and the other on bacteriological control of penicillin therapy. The greater part of the book is devoted to the clinical use of penicillin and covers the subject in great detail. Successive chapters deal with its use in generalized infections, bacterial endocarditis, chest infections, chest surgery, wounds and gas-gangrene, burns and plastic surgery, orthopædic surgery, hand infections, osteomyelitis, abdominal infections, obstetrics and gynæcology, sepsis neonatorum, brain and meningeal infections, venereal diseases, ophthalmology, otorhinolaryngology, dermatology, and dental and oral infections. There is also a chapter on "penicillin in animal diseases". The concluding chapter is entitled "penicillin and the general practitioner". In spite of the rapidity with which new information concerning penicillin is appearing, the work is well up to date. The wheel of destiny has indeed turned full circle since the medical profession failed to appreciate the significance of the now historic article in which Fleming reported in 1929 his discovery of penicillin. In that article the author, with prophetic foresight, remarked: "it may be an efficient antiseptic for application to, or injection into areas infected with penicillin-sensitive microbes". As the fulfilment of this prophecy, this volume will take a high place in the annals of medical literature.

The Causation of Appendicitis. BY A. RENDLE SHORT, M.D., B.S., F.R.C.S. Bristol: John Wright & Sons, Ltd. Pp. viii and 79. Price 10*s.*

THE author has long been interested in the search for the cause of appendicitis. He reviewed the subject in the *British Journal of Surgery* in 1920, and in this book he presents the same thesis with much added material. He starts with the marked increase in appendicitis that took place between 1895 and 1905. That the disease was rare in the preceding century is known but, as the author points out, it cannot be assumed that it was equally rare in Tudor and Stuart times. He concludes that King Stephen died of appendicitis, but in stating that no other King of England seems to have been a victim of the disease he forgets the illness and operation of King Edward VII on the eve of his coronation, events that were responsible for a boom in fashionable appendicitis and for two famous lines by the poet laureate of the day:—

> "Along the wires the electric message came,
> He is not better, he is much the same."

The book bears evidence of years of careful research, and is a storehouse of useful information not easily found elsewhere. The incidence of appendicitis at different periods in different countries and in different racial stocks is studied and reviewed in its relation to social and economic factors, and the many changes in diet that have occurred simultaneously. All these factors are susceptible of several interpretations, and the diagnosis of "appendicitis" alone means something very different in different countries and at different times. "Appendicitis" is the refuge of the diagnostically destitute, the stock-in-trade of the commercial, and the repute and integrity of any surgeon stands roughly in inverse proportion to that of appendicectomy in his practice. The difficulty of coming to any conclusion is shown by the figures from the Falkland Islands, where there were forty operations in 1936, twenty-two in 1937, five in 1938; as the author points out these figures might be attributed to the recent formation of a nutrition board, to the lack of any further appendices to remove, or to a change of surgeon. On the next page he points out that the national distribution of appendicitis varies with the degree of civilization; the Falkland Islands have a long lead, and the United States come second!

THE PRACTITIONER

ADVANCES IN MEDICINE

By LORD MORAN, *M.C.*, M.D.

President of the Royal College of Physicians; Physician to St. Mary's Hospital.

My task is to try to indicate the general trend of medical practice at the present time, and I shall begin by asking how far this will be affected by the Health Bill which has now been passed by the House of Commons. The feeling kindled by the transfer of ownership of the voluntary hospitals has diverted attention from the benefits which the reformation of the hospital service will bring. When the Bill becomes law the teaching hospitals will no more be handicapped by financial anxieties; the State will be responsible for their maintenance, and provision will be made so that they may be adapted and equipped for their first function, namely, undergraduate education. In the past, students have often spent their clinical years in a hospital, scarcely changed in structure since the days when laboratories were not held to be an essential part of an institution for the care of the sick. The medical school itself will have a special charter in recognition of the prime function of school and hospital, and its annual budget will be drawn up on a new scale.

It is generally supposed that the undergraduate teaching hospitals, which under the Bill are in a class apart, have been the favourites of fortune, but in my judgement it is the hospitals under the regional board which will most profit by the new conditions. All sizable hospitals in the Regions will probably be used for postgraduate education and in consequence their staffs will become a university service with all that this may mean in the way of stimulus and encouragement. From this it follows that the hospitals at Wolverhampton and Stoke, for instance, like the Queen Elizabeth Hospital in Birmingham, will have two functions, the local duty of caring for the sick and the national task of keeping medical practitioners up to date. And in the course of discharging the second of their duties these hospitals will establish a claim on central funds, for it will be the plain interest of Whitehall that postgraduate education shall not be starved financially. There will no longer be a distinction between voluntary and municipal hospitals; which is another way of saying that many municipal hospitals will be upgraded. The smaller voluntary hospitals may, it is true, have to prove to the Regional Board that they can efficiently carry out their duties. If they appear to be

NOTES AND PREPARATIONS

NEW PREPARATIONS

DIHALOQUIN is the name under which diodoquin, the new anti-amœbic drug *di-iodo-hydroxyquinoline*, will be placed on the market by Messrs. Savory & Moore Ltd., 61 Welbeck Street, London, W.1, from whom further particulars can be obtained. ·

STEROGYL-15 is a preparation of purified vitamin D_2. It is issued in single dose ampoules containing 600,000 I.U. vitamin D_2 for the massive dose treatment, by oral or parenteral administration, of rickets, tetany, lupus or tuberculous origin and other tuberculous complications as well as conditions due to vitamin D deficiency. Sterogyl-15 is available in single phials of 15 mgm. vitamin D_2 in 1.5 c.cm. oil for oral administration and in boxes of 4 phials of the same dosage for injection. The manufacturers are Roussel Laboratories Ltd., 95 Great Portland Street, London, W.1.

NEW APPARATUS ·

A NEW RETRACTOR FOR VARICOSE VEIN SURGERY —This instrument, which is a modification of a self-retaining retractor used in other branches of surgery, is so designed that it does not get in the way of the surgeon whilst operating. The angle of the shaft is adjusted so that the retractor lies flat on either side of the wound, and the jaws, the points of the teeth of which are so made that injury to neighbouring vessels may be avoided, give a firm grip of the tissues, so permitting lifting without slip. The retractor has been specially made for Mr. Rowden Foote, M.R.C.S., D.R.C.O.G., by John Bell and Croyden, Wigmore Street, London, W.1.

A MOTOR CAR FOR THE DISABLED

THE new "Larmar" car is a single-seater three-speed, four-wheeled car with an economical 2½ h.p. engine situated at the rear. The four wheels are independently sprung, and the car will cruise at 35 m.p.h., giving a petrol consumption of approximately 65 m.p.g. All controls can be arranged for either foot or hand, control of clutch, brake and throttle. The car measures 7 ft. 5½ in. in overall length and 2 ft. 4 in. in width, and will pass through a standard 2 ft. 6 in. gateway. The manufacturers have decided that in the first instance the car will be supplied only to disabled persons, and after such demand is satisfied will be made available to the general public. The selling price is £198, no purchase tax being paid by disabled persons. Further particulars can be obtained from "Larmar Cars" (Hall Car Sales Ltd.), Odeon Parade, High Road, North Finchley, London, N.12.

PENICILLIN THERAPY

"PENICILLIN THERAPY" is the title of a booklet published by Boots Pure Drug Co. Ltd., which gives an outline of the different conditions in which penicillin has proved beneficial, and details concerning the methods of usage. Copies of the booklet may be had on application to the Medical Department, Boots Pure Drug Co. Ltd., Station Street, Nottingham.

THE TREACHER COLLINS PRIZE ESSAY

UNDER the above title the Council of the Opthalmological Society of the United Kingdom has instituted a prize of £100, awarded triennially, for the best essay submitted on a subject selected by the Council. The prize is open to qualified medical practitioners of any nationality, but the essay must be written in the English language. The subject for the next award is "Nutritional Eye Disease", and the closing date for sending in essays is December 31, 1947. All essays should be submitted to the Honorary Secretary, Ophthalmological Society of the United Kingdom, 5 Racquet Court, Fleet Street, London E.C.4, from whom further particulars can be obtained.

OFFICIAL NOTICE

Surgeons' operating gowns.—Practitioners who need white operating gowns for obstetrical work, treatment of venereal diseases, operations or autopsies may now apply, stating particulars, for coupon equivalent certificates to the Ministry of Health, Whitehall, London, S.W.1, in Scotland to the Department of Health for Scotland, St. Andrew's House, Edinburgh, and those in Northern Ireland to the British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, enclosing a stamped, addressed envelope.

THE NUFFIELD FOUNDATION

THE first Report of the Nuffield Foundation, which covers the three years ending March 31, 1946, contains a summary of the aims, objects and policy of the Foundation, which, in brief, are the promotion of optimum health by research, prevention and cure of disease. The total grants made by the Foundation during the three years amounted to a sum of £882,820 : industrial health, dental health, scientific and social research, research on the subject of ageing and on child health are among the three years' activities.

reconstruction of the methods of teaching, of examining and of writing textbooks.

So far as the efficiency of a doctor is dependent upon the help of science it may be said that the whole position has been transformed since I was a medical student: in those days surgery appealed to many of the most ardent spirits; it did something, whereas a physician was forced too often into a position of intelligent observation. Nowadays a medical ward, like a surgical ward, is full of patients who expect to get quite well, and the number of men who wish to specialize in medicine reflects their growing faith in the physician's opportunities. Three hundred and forty-one candidates presented themselves for the membership of the Royal College of Physicians in July of this year, and this examination is held four times a year. Penicillin is after all only the last, although the most triumphant and the most dramatic, example of the arming of the modern physician. Yet there are some who are still sceptical of the scientific method as applied to clinical medicine, and there are others who have been critical of the search for exactitude in diagnosis, which is, and I hope always will be, the beginning and the end of clinical training. We can at any rate all subscribe to a warning not to neglect the examination at the bedside.

PENICILLIN

The supply of penicillin is now ample; the production of 6,000 mega units in June of last year rose to 300,000 units in June this year. We are no longer importing penicillin; we are exporting it to other countries. Penicillin a year ago was only 30 per cent. pure; the purity has now risen to 80 per cent. Pure penicillin has been made and, although it is not yet in general use, it will be of service in those conditions for which the irritation due to impurities is a disadvantage, as in infections of the eye. Incidentally, when pure penicillin is available inhalations will lose their unpleasant mouldy smell.

Dosage.—If the dose of penicillin is insufficient there is a real danger of breeding a strain of resistant or insensitive organisms. It is a sound general rule to double the dose if in doubt; an overdose is impossible. Whereas 15,000 units every three hours has been commonly given, much larger doses are now the rule—for instance, 200,000 twice daily or 500,000 once in the day; the average number of units given in the twenty-four hours may be put at 250,000. The rapid absorption and elimination by the kidneys has made frequent injections inevitable; the rate of excretion cannot be changed, but if penicillin is injected in a mixture of arachis oil and beeswax its rate of absorption is retarded and a depot is formed at the site of the injection. In this way a blood level may be maintained for eighteen to twenty-four hours, instead of six hours with the same amount of penicillin in saline.

Of other methods of administration little need be said: penicillin given by the mouth is destroyed in the stomach. As an inhalation it has now had a fair trial. A spray is ineffective, but the fine vapour given by many asthma

handicapped by their size they may be asked to work in conjunction with some other institution: in short, if a hospital is not able, either on account of the number of its beds or the experience of its staff, to discharge all the duties of a general hospital, the Regional Board may decide what function it can best serve in the new service. The dispassionate observer cannot fail to conclude that a planned hospital service of this kind is a major advance, however much the interests of a particular institution may tug at his heart. If it did no more than quicken the transformation of many municipal institutions into hospitals second to none—a process which has been going on for some years—and bring about the decentralization of the younger consultants, it must have a most salutary effect.

The proposals in the Bill which concern general practice are more open to criticism. Many practitioners fear that the remuneration of doctors in the new service in part by a basic salary, coupled with the abolition of the custom of buying and selling practices and some measure of direction where they work, will lead in time to a whole-time medical service. There may be substance in these fears. If there is, we have still to ask whether a whole-time service would necessarily make for slackness and inefficiency. To that question there is no satisfactory answer; no-one can tell what will happen if and when the average practitioner no longer has a financial incentive to bring the best out of him. It is plainly irrelevant to cite the analogy of existing services in which the problem of keeping men keen has been bound up with the difficulty of providing them with adequate opportunities of practising their profession. This may be said: the efficiency of the new service will depend in the last resort upon its ability to continue to attract the same type of man who in the past has made the reputation of the profession. No reformation of the hospital service can save the situation if the rank and file lose their pride of craftsmanship and if the profession of medicine is no longer able to compete with other callings in attracting the man of promise.

The efficiency of a doctor depends upon the intelligence with which he practises his art and the weapons that science has placed in his hands. The former will always be governed in the main by the ability of the boy entering medicine, but his training at the medical school can do something to excite his curiosity and to develop his natural powers. The Goodenough Report and the Report of the Royal College of Physicians were both concerned with medical education. The members of the Goodenough Committee were perhaps unduly impressed by what can be done by organization and by financial support. It is true that their proposals under these heads will be very helpful to the schools, but no great educational document has ever been printed which was not on fire with the faith of the writer. The committee of the College was a younger committee—it had no faith in tinkering —it believed that there was something radically wrong with our present methods of medical education and looked for the remedy in a fundamental

it an adequate trial in clinical medicine: meanwhile this may be said, that it appears to have many advantages over remedies previously tried in the treatment of tuberculosis.

THE SULPHONAMIDES

No spectacular advances have been recorded in the use of the sulphonamides. Sulphamerazine, a new compound from America, has had a limited trial in this country with encouraging results but there is no evidence that it is more active than sulphathiazole, sulphadiazine or sulphamezathine. Sulphamerazine can, however, be administered at less frequent intervals, every six or eight hours instead of four-hourly as in the case of most of the other sulphonamides. If I may venture a personal opinion (and I know that Sir Lionel Whitby shares this view) sulphamezathine is the most useful of these compounds, since unpleasant symptoms (nausea, vomiting, giddiness) are rare and it does not form insoluble crystals in the urine. Gradually the fields of usefulness of penicillin and of the sulphonamides are being more exactly mapped out. In *B. coli* infections the sulphonamides are effective whereas penicillin is ineffective, but in the coccal infections we mainly rely on penicillin.

TRANSDIAPHRAGMATIC RESECTION OF THE VAGUS NERVES FOR PEPTIC ULCER

The treatment of peptic ulcers by the physician has lost repute with some observers on account of the frequency of relapses. Indeed, apart from the physical deformity which may follow the cicatrization of an ulcer, the case for surgery in the treatment of peptic ulcers rests on this tendency to relapse after the ulcer has been healed. Transdiaphragmatic resection of the vagus nerves in fifteen patients was carried out by Moore and others working at Boston. A sizable portion of both vagus nerves was resected and steps were taken to prevent regeneration. The final value of this method must await the passage of time, but the immediate clinical results justify at least a hope that this operation will avoid the return of the ulcerating tendency which has up to the present time marred the records of every method of treatment.

THE REFRACTORY ANÆMIAS AND FOLIC ACID

Folic acid is a vitamin which has recently been separated from that sub-division of the vitamin B complex known as the *L. casei* factor. Its relationship to the liver principle used in the treatment of pernicious anæmia is not clear. Cases have been reported of macrocytic anæmia which did not respond to folic acid but did respond to liver extracts containing only a minimal amount of folic acid. It would therefore appear that folic acid is not the complete anti-anæmic factor.

inhalers relieves acute bronchitis; in chronic bronchitis the relief is only temporary.

Penicillin is not a cure for *the common cold;* it prevents the sequelæ of a cold: the purulent stage is often aborted and so the life of a cold is cut short. It may be used to prevent infection before and after *abdominal operations.*

Subacute bacterial endocarditis was a fatal disease before Fleming's discovery; now about 70 per cent. recover; a high percentage when it is remembered that patients with damaged hearts may die from heart failure even if the causative organism is killed by penicillin. The dose required is 500,000 units daily for one month.

Ophthalmia neonatorum can be cured in twelve hours with a course of penicillin—2,500 units per c.cm., as eye drops, applied at given times.

In using penicillin in *skin affections* it is essential to establish that the infected organism is sensitive to penicillin, which can only be done with the help of a bacteriologist, and then it is necessary to use an adequate dose of penicillin. The common practice of under-dosage only breeds resistant staphylococci. Penicillin is as effective in suppurating lesions as it is ineffective in dry eczema, adult pemphigus and psoriasis. As the field of usefulness of penicillin is defined with more precision, gratitude for this benefaction increases.

p-AMINO-BENZOIC ACID AND STREPTOMYCIN

Scrub typhus.—The field of disease which responds to chemotherapy is growing. Up to now there has been no remedy worth the name for rickettsia infections, but it seems probable that in para-aminobenzoic acid, which inhibits the action of sulphanilamide, an effective remedy has been found, although no claim is advanced that its action is comparable to that of penicillin and the sulphonamides in bacterial infections. In patients with scrub typhus treated with *p*-amino-benzoic acid the severity of the symptoms was less, the period of convalescence shorter, complications such as bronchitis were less common, and the mortality was reduced. The drug was given by mouth, as a powder partly neutralized with sodium bicarbonate to lessen gastric irritation. The initial dose is 8 gm., followed by 3 gm. every two hours, which gives a blood concentration of 30 to 60 mgm. per 100 c.cm. within two days.

Tuberculosis.—The Harben lectures delivered by Dr. William Feldman of the Mayo Foundation were concerned with the vulnerability of the tubercle bacillus to certain specific drugs. The protection conferred by streptomycin on guinea-pigs infected with tuberculosis raised hopes which have yet to be confirmed in the treatment of human beings. The number of cases treated is small and the actual results although promising are not conclusive, but it is something to have learnt that the tubercle bacillus is vulnerable to a drug and that this drug can be safely administered to human beings. It will be many months before there is enough streptomycin to give

as radium. The element is made radio-active by being bombarded with neutrons given off by a special machine, the cyclotron. The radiations can be detected by a specially devised instrument or counter. A single illustration may make this clear. Phosphorus is taken into the body, for example, as milk. Before the splitting of the atom we knew that there was phosphorus excreted in the urine and stools, and we also knew that phosphorus was present in bones, brain, glands and liver; but we could not follow the phosphorus from its ingestion to its excretion. Now we can take radio-active phosphorus, and its path in the body is revealed by detecting the radiations from it, just as a burglar may be betrayed by his fingerprints on the furniture or windows. The various organs can actually be examined at specified intervals after swallowing the phosphorus and the actual amount ascertained of the ingested radio-active phosphorus present in each organ, and so the whole story of the metabolism of phosphorus in the body can be traced.

This discovery of artificial radio-activity will have a twofold impact on medicine. On the one hand, as described above, the artificially radio-active substances can be used as tracer elements in solving many of the problems of metabolism; on the other hand, these same substances can be used for direct treatment of different types of disease, either by ingestion or by injection into the blood stream. It is known that certain substances have a specific affinity for certain organs and that they will be concentrated in such organs in a short time after ingestion. For example, phosphorus is found especially in lymphoid tissue, and if radio-active phosphorus is given in leukæmia it acts on the leukæmic tissue like radium or X-rays applied externally. Again, in polycythæmia the radio-active phosphorus kills the immature erythroblastic tissues, so that a cup of radio-active phosphorus taken once a week may replace the application of X-rays to the spleen. To follow the metabolism of chemical substances in the body by these tracer methods has been called a new approach to physiology. In this field of nuclear physics the imagination can hardly follow its boundless possibilities.

VENEREAL DISEASE

I am indebted to Dr. G. L. M. McElligott for the following notes on the use of penicillin in gonorrhœa and syphilis.

Gonorrhœa.—Penicillin is now the drug of choice in all cases in which the infection is of gonococcal origin. It is useless in non-specific urethritis. A high percentage (80 to 90 per cent.) of rapid and permanent cures follows adequate treatment. There is a difference of opinion as to how much treatment is necessary, but most workers now give at least 200,000 units, in divided doses, over a minimum period of ten to twelve hours, in contrast to the 100,000 units thought adequate eighteen months ago. Results in women and female children do not seem to be as good as in men, and metastatic complications, e.g. arthritis, do not respond dramatically,

Folic acid is not as yet obtainable in England, although small quantities have been distributed to various centres in this country. But it is a substance of known composition, which has recently been synthesized by Angier, and it should not be long before it is produced on a large scale. When that happens it may well supersede liver extracts in the treatment of all anæmias in which it is found to be useful, since liver extracts have to be biologically tested on patients with pernicious anæmia. Spies (1946) and others have reported satisfactory results in various types of macrocytic anæmia. A minute daily dose, 20 mgm. by mouth, appears to be sufficient and the response is comparable in every way with that obtained by the treatment of pernicious anæmia with a potent liver extract. These results have recently been confirmed in this country (Wilkinson, Israëls and Fletcher, 1946), and it has been shown that synthetic folic acid will bring about remissions in patients with true Addisonian pernicious anæmia, and that the responses seem in " every way " comparable to those obtained with the best pre-war liver extracts. It would seem then that folic acid can safely be substituted for liver extracts, at least in the early stages of treatment of true pernicious anæmia. The maintenance dose has not yet been worked out, and the supplies of folic acid necessary for this purpose are not yet available.

Besides pernicious anæmia, the macrocytic anæmias of infancy, of sprue and that due to malnutrition have responded to treatment, whilst cases of aplastic anæmia and leukæmia have shown no response. It is well to bear in mind that the case reports published concern patients who have not been treated for a prolonged period, nor is it yet clear whether folic acid therapy, like liver therapy in pernicious anæmia, has to be continued indefinitely or whether in some, at any rate, of the conditions treated, it may be regarded as curative.

Carruthers (1946) has reported a rapid improvement in six cases of chronic diarrhœa of varied etiology treated with folic acid. He suggests that any long-standing diarrhœa may cause folic acid deficiency and that this in turn may prevent recovery from the diarrhœa. The need for folic acid apparently persists after the diarrhœa is cured, as relapses occurred the day it was withdrawn.

NUCLEAR PHYSICS IN MEDICINE

No attempt to summarize medical progress in the past year would be complete without mentioning the impact of nuclear physics on medicine; it is a fascinating story which, by those not engaged in this field, can at present only be read in a translation. I must here be content with a mere reference to the subject. As a result of the latest researches in nuclear physics it has been found possible to make all the common elements radio-active, that is, for a short period the radio-active element gives off radiations comparable in type to those normally given off by radio-active substances such

ADVANCES IN SURGERY

By J. PATERSON ROSS, M.S., F.R.C.S.

Professor of Surgery, University of London; Surgeon and Director of Surgical Unit, St. Bartholomew's Hospital.

IN reviewing surgical progress it must always be a matter of special interest to note the circumstances which paved the way for a new approach to an old problem, or which suggested some fresh field for surgical enterprise. Specialism and team work favour advances in surgery, but it must be understood that many of the modern procedures would be more appropriately termed "combined operations", for the problem may be attacked at the same time by two or more teams, each with its own leader and its separate organization.

COMBINED OPERATIONS

The idea of two surgeons working in collaboration was carried into practice before the war in the operation for abdomino-perineal excision of the rectum, and in many hospitals it is now the standard procedure. Whilst it has stood the test of time, this method carries its own special risk, for it seems that there is a limit to the amount of surgical trauma the body is able to withstand in a given period of time. To undergo two big operations simultaneously is a considerable strain upon the patient's endurance, and special measures have to be taken to combat shock.

There is something to be said for adopting a similar procedure in total cystectomy. The most difficult step in this operation when it is done entirely from above is the separation of the prostate and the base of the bladder from the rectum, and this could be undertaken with more direct access by a second surgeon working from the perineum.

It was the policy of all the medical services during the war, not only to form a large number of surgical specialist units, but also to group these units together for mutual assistance. The benefits which this collaboration bestowed upon the wounded was clearly shown by the astounding results achieved from the Forward Surgical Units to the Base Hospitals; but the benefit to surgery may be even greater, provided that this close association of specialists, learnt in war, can be carried on into peace-time organization, more especially in postgraduate surgical training.

The most notorious and the most successful of the specialist combinations was the Unholy Trinity of Neurosurgical, Faciomaxillary and Ophthalmic Units. Head wounds often involved the face and the eye as well as the scalp, skull, and brain; the plastic surgeon helped the neurosurgeon to fashion scalp flaps, and the debt was repaid when nasal injury was complicated by cerebrospinal fluid rhinorrhœa; the help of the ophthalmologist was often needed by both of the other specialists; and they all learned from one another.

although the urethral infection usually does so. Late relapses occasionally occur and tests must be made at least three months after treatment. A blood test for syphilis should also be done three months after treatment, since there is some slight danger of a concurrent syphilitic infection being masked or modified while it is incubating. Oil-wax suspensions of penicillin (e.g. in 4 per cent. beeswax in peanut oil) are slowly absorbed from the injection site and cause a prolongation of the penicillin blood level. They are useful for out-patient work, when the patient can only attend once or twice daily.

Early syphilis.—Follow-up findings in many thousands of cases in British and American Forces treated with 2,400,000 units of penicillin (40,000 units given four-hourly for seven-and-a-half days, i.e. sixty injections) indicate that the following relapse rates may be anticipated:—

Primary syphilis	W.R. negative	5 per cent.
Primary syphilis	W.R. positive	10 per cent.
Secondary syphilis	W.R. positive	15 to 30 per cent.

There is now a tendency to increase the total dose to three or even four mega units and the period of administration to ten days, and most workers in this country give one course of ten injections of N.A.B. or mapharsen and bismuth as well. A minimum follow-up of two years is necessary and the C.S.F. must be examined before discharge. Relapses, serological or cutaneous, usually occur during the first year's observation. Positive blood tests may take as long as six months to revert to negative after treatment. Out-patients may be given 500,000 units in oil-wax suspensions daily or 250,000 units twice daily. Results so far are promising.

Late syphilis.—Visible lesions, e.g. skin gummas, are rapidly resolved by penicillin, although positive blood tests usually remain so. Owing to the danger of cardiac reactions it is unwise to begin the treatment of late syphilis with penicillin: a month's course of bismuth and iodine is always desirable first. There is a growing feeling that all cases of late syphilis, except possibly advanced cardiovascular cases, should have penicillin in addition to some "insurance" treatment with the more time-honoured drugs.

References

Carruthers, L. B. (1946): *Lancet*, i, 849.
Spies, T. D. (1946): *Ibid.*, i, 225.
Wilkinson, J. F., Israëls, M., and Fletcher, F. (1946): *Ibid.*, ii, 156.

The radical treatment of *chronic osteomyelitis* can succeed only when the disease is so placed and is of such an extent as to permit of its complete excision. Operation is performed in multiple stages, always with penicillin protection (Robertson and Barron, 1946).

At the first stage, extensive excision of all diseased skin, scar tissue and infected bone is carried out and the vascular bone and soft tissue thus exposed is covered with split skin-grafts. When this wound has been healed for four weeks the next stage may be undertaken, in which the soft tissues are replaced by some form of flap which will provide a good thickness of supple healthy cover to the bone defect: a process which may itself involve several "stages". Finally, eight weeks after the completion of the soft tissue replacement the bone repair is completed by grafting; the bone cavity may be filled up by a combination of onlay and cancellous chip grafts, together with muscle advancement, if necessary.

The secret of success lies in delaying any attempt at bony reconstruction until a sound covering of skin and soft tissue has been provided over the affected area of bone.

Enough has been said to indicate how advances may be made through the collaboration of specialists. The moral is that the specialist cannot make his maximal contribution to the advancement of surgery if he works in isolation.

PROSTATECTOMY

The patient whose prostate is enucleated is exposed to risks from shock, hæmorrhage, renal failure, and infection. Of these the most difficult to control is infection, which may arise from catheterization but is inevitable with suprapubic drainage of the bladder. The new techniques introduced by Wilson Hey and Millin have this advantage in common—they are both practised without suprapubic drainage and thus increase the patient's comfort and shorten his convalescence.

By Wilson Hey's method (1945) "almost finicky" standards of asepsis are aimed at, the prostate is removed digitally through a suprapubic cystostomy approach, all tags are removed and great care is taken to stop all bleeding with the diathermy cautery. A tube 1 mm. thick with a lumen diameter of 6 mm. is passed from the bladder along the urethra for drainage and the bladder is closed in three layers. The urethral tube remains for four days, by which time all oozing should have ceased and the patient should be able to pass urine. ·

Millin's operation (1945), which is described in greater detail by R. H. O. B. Robinson on page 285, has the added advantage of never opening the bladder at all. The retropubic approach was suggested by the excellent exposure which is obtained of the front of the prostate in the course of total cystectomy. The operation is done under vision, hæmorrhage from the prostatic bed is arrested, a catheter is passed into the bladder and finally the incision in the prostatic capsule is sutured. The catheter is removed on the fourth day after operation and the average time in hospital is much shorter than after any form of open prostatectomy with suprapubic drainage. Although there is a risk of post-operative

TRANSTHORACIC GASTRECTOMY

Collaboration between the "general" surgical specialist and the thoracic surgeon has led to the modern treatment of carcinoma of the lower œsophagus and the cardiac end of the stomach, and many general surgeons now consider that the only correct approach to carcinoma of any part of the stomach which demands total gastrectomy for its cure is through the chest. There is still the old problem of how to make a safe junction with the œsophagus which lacks a serous coat, but ingenious methods have been devised of bedding its terminal portion in the peritoneum-lined abdominal viscus to which it is to be anastomosed. When the growth is in the œsophagus and the stomach itself can be used for the junction the procedure is simpler than after total gastrectomy, when the mobilization of a sufficient length of jejunum with an adequate blood supply is a matter of greater difficulty, in which surgical judgement and experience are the only safeguards against a fistula.

For irremovable growths at the lower end of the œsophagus Allison (1946) has performed œsophago-jejunostomy as a palliative measure which is clearly preferable to gastrostomy.

OSTEOMYELITIS

The contribution which plastic surgery can make to orthopædics is now so well recognized that in planning the civilian surgical services it is accepted that any first-class orthopædic centre should have a plastic unit working in close association with it. During the war, the orthopædic surgeon who was faced with extensive skin and soft tissue loss in addition to osseous injury found the help of the plastic surgeon invaluable, and this experience is now being applied to the treatment of chronic osteomyelitis.

Although it now seems almost redundant to mention penicillin in this connexion it must always be remembered that had it not been for this antiseptic "umbrella", the advances in the treatment of acute and chronic bone infection which have been made under its protection would never have been possible.

It is now established that the mortality rate of *acute hæmatogenous osteomyelitis* has been reduced to about one-fifth of the previous figure by penicillin therapy, and that if penicillin can be given during the first few days, resolution of the infection may render operation unnecessary. It is unwise to combine operation with penicillin in this early stage of the disease, because resulting sequestration of bone with sinus formation delays healing, and the only advantage gained by penicillin is freedom from toxæmia. If, however, when the condition is too far advanced for resolution to occur, local treatment is confined to immobilization, and penicillin is relied upon to deal with the infection, the only operative treatment required later on will be the drainage of an abscess or the removal of a sequestrum. A week after this operation the wound can be closed by secondary suture, the total duration of the illness being thus greatly shortened.

in the days before the prostigmin requirements and other details of pre- and post-operative treatment were known, called for courage in execution as well as confidence in the rational basis of the method, and these problems of the pioneers are clearly described by Keynes (1946) in the account he gives of his first fifty thymectomies. Eight patients died shortly after the operation. Of thirty-three who have been observed for long enough to make a reliable estimate of the effects of thymectomy, nine are well, eleven greatly improved, eight somewhat improved, and five are no better. Keynes concludes that the younger the patient and the shorter the history the better the outlook; tumours of the thymus carry a poor prognosis.

Curare.—Although it is thought that in myasthenia the thymus is producing a substance which interferes with the mechanism whereby acetylcholine activates voluntary muscle, precise details about the upset of this normal chemical process are as yet undetermined. It is probably true to say that the action of the poisonous substance in myasthenia resembles that of curare, which has been employed for some time by psychiatrists to mitigate the undesirable effects of convulsive therapy and is now used as an adjuvant in anæsthesia.

Curare must not be employed as an alternative to, or to mask errors in, ordinary anæsthetic technique (Cullen, 1945). Although the drug has no effect on heart muscle, it was difficult at first to determine the dose which would paralyse voluntary muscle and yet would not affect unduly the diaphragm and the peripheral circulation. In order to avoid overdosage it should be used only to obtain that extra relaxation which may be so valuable after the best possible has been attained with ordinary anæsthesia. In emergency, prostigmin is an effective antidote to curare.

SURGERY OF LARGE ARTERIES

The most startling of all the innovations are the operations upon the aorta for coarctation and upon the pulmonary arteries for the congenital malformations associated with cyanosis. The circumstances of warfare were found to be unfavourable for practising on any considerable scale the various suggestions which were made for improving upon the standard treatment of arterial wounds. It is practice in the experimental laboratory which is directly responsible for these latest advances in arterial surgery, since it was by gaining familiarity with the technique of vascular anastomosis in lower animals that surgeons have acquired the necessary experience to give them confidence in understanding what must otherwise have been an unduly hazardous procedure in human surgery. The surgical experimental laboratory at Johns Hopkins has long been regarded as one of the foremost veterinary hospitals in the world, and its contributions to the alleviation of human as well as of canine disease must be. a hard nut for the antivivisectionists to crack.

hæmorrhage into the bladder and also of late stricture formation, this operation must be regarded as the best-planned attempt yet made to apply sound surgical principles to prostatectomy.

PANCREATECTOMY

The many ingenious methods of restoring the alimentary canal and the bile passages after resection of the duodenum and the head of the pancreas, from Whipple's earliest ventures in this field up to the present day, have been critically reviewed by Orr (1945). It is a wonderful record of what is now being achieved to combat a disease for which until recent years palliation alone seemed possible; yet the ideal is still for pursuit. Metastases keep the survival rate down to a disappointingly low figure, and it cannot even be shown as yet that radical surgery gives better results than conservative operation.

The question whether to operate in one or two stages has not been decided. The handicap of adhesions in multiple-stage operations is the chief argument for a single-stage procedure, but the deciding factor must always be the general condition of the jaundiced patient, and statistics favour two stages. If only the operation could be done early in the disease more patients would be curable and more operations could be undertaken in one stage.

In order to avoid ascending infection of the biliary tract and to obtain a better flow of bile, anastomosis of the common bile duct to the jejunum is considered preferable to any form of cholecystenterostomy. But a decision has not been reached as to whether the stump of the pancreas should be implanted into the intestine or merely oversewn. The latter carried the risk not only of pancreatic fibrosis but also of liver damage; with implantation there is the risk of pancreatitis and fistula formation; but which risk is the greater is still undetermined.

THYMECTOMY AND CURARE

The realm of surgery is already so vast that an entirely new idea which extends its scope still further causes not merely a sensation but a thrill. The treatment of myasthenia gravis by thymectomy engages the interest of the physiologist, the pharmacologist and the neurologist, as well as of the surgeon, and may well lead to a better understanding of normal as well as other forms of abnormal muscular activity.

The occasional association of a tumour of the thymus with a myasthenic state was noted many years ago, and it is now thirty-five years since an attempt was made to remove the thymus for myasthenia. The approach was from the neck, but this dangerous and incomplete operation was soon abandoned and nothing more was heard of thymectomy until Blalock in 1941 published his experiences of six thymectomies in which access was gained by splitting the sternum. To undertake a big operation on a myasthenic patient

sympathectomy for arterial disease and injury. French surgeons, following Leriche, are convinced that sympathectomy should be performed as early as possible after wounds or ligation of large arteries; and there is good evidence that it improves the usefulness of limbs in which a main artery has to be sacrificed in the treatment of arterio-venous fistula. Grimson (1946), in a thoughtful review of his own material, raises once again the question of pre- or post-ganglionic section, and suggests that there is much to be said for a return to post-ganglionic sympathectomy.

CLOSURE OF SKULL DEFECTS

A decision has not been reached about the relative merits of autogenous bone grafts, and acrylic resin or tantalum plates for the closure of defects in the skull. Tantalum is considered to be the easiest to fashion, but its opacity to X-rays may be a serious drawback if intracranial suppuration supervenes and radiography cannot be employed in localizing the focus of infection.

If the wound or disease which caused the bone loss was associated with infection, time must be allowed for complete resolution to occur before any kind of closure is undertaken. The insertion of a plate too early is a common cause of suppuration which continues until the foreign material is removed. Another cause of trouble is failure to provide an adequate thickness of sound skin to overlie the graft or plate. If this covering is too thin, or is scarred and unhealthy, minor injury or even an insect bite may lead to disaster. It has been found that if cancellous chips alone are used to fill a gap the bone may be absorbed. Under proper conditions acrylic resin or tantalum plates can give excellent cosmetic results, but it must be admitted that bone is safer and, if skilfully prepared, grafts from ribs or ilium can be made to replace any part of the contour of the skull.

References

Allison, P. R. (1946): *Proc. roy. Soc. Med.*, **39**, 415.
Blalock, A. (1941): *J. Amer. med. Ass.*, **117**, 1529.
——, and Taussig, H. B. (1945): *Ibid.*, **128**, 189.
Cullen, S. C. (1945): *Surgery*, **18**, 45.
Grimson, K. S. (1946): *Ibid.*, **19**, 277.
Gross, R. E. (1945): *Ibid.*, **18**, 673.
Hey, H. W. (1945): *Brit. J. Surg.*, **33**, 41.
Keynes, G. L. (1946): *Ibid.*, **33**, 201.
Millin, T. (1945): *Lancet*, ii, 693.
Orr, T. G. (1945): *Surgery*, **18**, 144.
Robertson, I. M., and Barron, J. N. (1946): *J. Bone. Jnt. Surg.*, **28**, 19.

CONGENITAL PULMONARY STENOSIS

The congenital malformations which are suitable for treatment are those in which the pulmonary artery is small, with or without associated abnormality of the aorta and defective development of the interventricular septum. There should be clinical and radiological evidence of decrease in the pulmonary blood flow. As Blalock and Taussig (1945) point out, the volume of blood which reaches the lungs for aeration is a most important factor in the production of cyanosis, and operation on these cyanosed patients is undertaken with the object of anastomosing a systemic artery to a branch of the pulmonary artery so that there may be an increased flow of blood to both lungs.

For certain conditions the innominate artery has been joined to the right pulmonary artery, but an end-to-side anastomosis between the left sub-clavian and left pulmonary arteries has more commonly been indicated. There is an immediate improvement in the patient's colour and exercise tolerance, and time alone will tell whether or not the alteration in the circulation will have any undesirable effects. Considering how recently ligation of a patent ductus arteriosus was hailed as a surgical triumph, it is odd that surgeons should now be invited to regard the formation of an artificial ductus as a still greater achievement!

COARCTATION OF THE AORTA

Sometimes the clinical manifestations of coarctation of the aorta are not serious enough to demand treatment; but if the lumen is very much narrowed or actually obliterated the hypertension in the upper part of the body and the poverty of the circulation in the legs demand that something shall be done to prevent death from cardiac failure or cerebral hæmorrhage.

An extremely interesting account is given by Gross (1945) of his early experiments on anastomosis of the aorta, and of the first two operations for excision of the narrowed segment in patients with coarctation. The first was performed on a five-year old boy and, although end-to-end anastomosis was successfully carried out, the clamps were removed too quickly and the sudden opening up of the huge vascular bed in the lower part of the body caused cardiac dilatation and death within a few minutes. In the second, which was performed on a girl aged twelve years, when the junction had been made the distal clamp was first removed; then with the table tilted into the Trendelenburg position, and with blood running fast into a leg vein, the upper clamp was gradually released, ten minutes being allowed for its complete removal. The manœuvre succeeded, and subsequent experience has justified the adoption of these precautions, with the addition of penicillin, and repetition of transfusion if necessary. Heparin or dicumarol were not used. Operation did not result in an immediate restoration of the circulation to normal. The blood pressure fell slowly in the arms and rose slowly in the legs, and it was several days before conditions were stabilized.

SYMPATHECTOMY

There is now a great deal of clinical material ripe for analysis which should provide clearer indications than have so far been available of the value of

emphasize in the post-war years of scarcity the need for ensuring, by the continuation of the food priorities and supplements, that the nutritional standards of the mother are safeguarded.

SULPHONAMIDES AND PENICILLIN

Puerperal sepsis.—The great reduction in the mortality rate from puerperal sepsis during the past ten years (from 2 per 1000 total births in 1934 to 0.6 in 1945) is by common acceptance due to the *sulphonamides*. There is reason to believe (Kenny, 1945; Colebrook, 1946) that there has been no corresponding reduction in the total number of cases of puerperal infection. Colebrook states:—

"The control of streptococcal infection is still a major issue in obstetrics. Although the mortality from these infections is much reduced, their incidence is still too high."

The reduction in this incidence can be achieved only by better obstetric practice. This implies the encouragement of normal labour and the adoption of an effective aseptic and antiseptic technique. Recently attention has been directed (Colebrook, 1946) to the part air-borne infection due to dust may play in puerperal sepsis. This serves to emphasize still further the importance of the antiseptic ritual in midwifery. Each time the vaginal opening is exposed during the vulnerable period, that is, during labour and during the early puerperium, a free use of the suitable antiseptic is indicated.

In the majority of cases of puerperal sepsis due to the A group of hæmolytic streptococcus and those due to *B. coli* the sulphonamides are effective. There are, however, resistant strains of these bacteria and a not inconsiderable number of cases of puerperal sepsis are due to other bacteria which, whilst resistant to the sulphonamides, respond to penicillin. These are *Clostridium welchii* and *Staphylococcus aureus.*

James (1945) has reported a small series of cases of infection with the A group hæmolytic streptococcus, in one of which cerebral thrombophlebitis was present, which responded well to penicillin after unsuccessful treatment with sulphonamides: 15,000 Oxford units were given three-hourly and continued for from three to seven days.

Cases of *Clostridium welchii* infection also treated successfully with penicillin have been reported by Hudson and Rucker (1945).

It is too early to assess the relative value of *penicillin* in puerperal sepsis. Whilst its great value in analogous infections in the general medical and surgical field has been established, its strict reservation for war purposes during recent years has restricted the opportunities for its trial in obstetrics. But an important place in this sphere may confidently be predicted for it, and there are several obvious advantages which it possesses over the sulphonamides. It is free of the toxicity, both immediate in the shape of nausea and remote in the shape of agranulocytosis, which hampers the free use of the sulphonamides. It also eliminates the risk of the crystalline deposits in the kidney tubules with damage to kidney function found with

ADVANCES IN MIDWIFERY

By JAMES YOUNG, D.S.O., M.D., F.R.C.S., F.R.C.O.G.

Professor of Obstetrics and Gynæcology, University of London; Director, Unit of Obstetrics and Gynæcology, British Postgraduate Medical School.

NUTRITION DURING PREGNANCY

DURING recent years much attention has been given to the influence of the nutrition of the mother during pregnancy, on her own health and on the well-being of the infant. It has been computed that during pregnancy the daily intake of the mother should not drop below 2500 to 2700 calories. It has long been known that during pregnancy extra demands are made on the mother's reserves of vitamins. With reserves which seem to be adequate to maintain her in apparent health in the non-pregnant state she may, however, develop severe manifestations of deficiency (osteomalacia, rickets, beri-beri) if she becomes pregnant. But it was believed until comparatively recently that the child was able to secure its own safety, even with grave maternal deficiency, by its capacity to dig into the maternal stores. This view is no longer tenable.

Investigations carried out in Toronto in 1941, suggest that pregnant mothers on a defective diet are exposed to greater risks of toxæmia and have a higher incidence of abortions, premature births and still-births. Similar conclusions were suggested by the People's League of Health investigation (1942) in 5,000 antenatal women in London. Burke, Harding and Stuart (1943) in America showed that when the average total protein of the mother's daily dietary is under 45 gm. the average birth weight of boys is 6 lb. 8 oz. and of girls 5 lb. 14 oz. The birth weight of boys increases to 9 lb. 2 oz. and of girls to 8 lb. 8 oz. as the average total protein rises to 85 gm. or more.

In the past, many doctors have been in the habit of advising their pregnant patients to restrict their intake of protein. In my opinion there never has been the least evidence to support such a view. Recent work indicates that, especially during the last months of pregnancy, the needs for protein are greatly increased—up to 50 per cent. Further, this protein should be in the main (up to 66 per cent.) of animal nature—milk, meat, eggs, cheese, poultry and fish (Williams, 1945). The remaining proteins are supplied from vegetable sources—vegetables and cereals.

In the Summary Report of the Ministry of Health for the year ended March 31, 1944, it has been claimed that the remarkable health experience of mothers and children during the war years has been in considerable part due to improved maternal nutrition. The maternal death rate and the still-birth, neonatal and infantile death rates have dropped to record low levels. These record figures have been achieved despite those influences arising from the war that make for family instability, e.g. disrupted homes, acute housing shortage and the wholesale entrance of women into industry. It has been claimed that by contrast they serve to underline the direct influence which the improved economic and nutritional standards have exerted on the reproductive health of the mothers. They serve further to

There is some evidence that penicillin may be of value in the treatment of prenatal *syphilis*, and it would seem that the drug when administered to the mother reaches the fœtal circulation in effective concentration (Woltz and Zintel, 1945; Parks, 1945). The dose recommended by Lentz and his co-workers (1944) for the pregnant syphilitic woman is 2,400,000 Oxford units given by intramuscular drip over eight days.

Mastitis.—As breast abscess is generally due to infection with staphylo-cocci it is suited for treatment with penicillin. It is claimed that timely administration of the drug in a dosage of 25,000 Oxford units every three hours for three days, followed by 15,000 units three-hourly for two days, is effective in preventing abscess formation (Hodgkinson and Nelson, 1945).

THE RHESUS FACTOR: ERYTHROBLASTOSIS FŒTALIS

The discovery in 1940 of a hitherto unknown blood agglutinogen by Landsteiner and Wiener has thrown new light on certain diseased states in mother and child. This agglutinogen was called Rh because it was found to be present in the serum of rabbits (or guinea-pigs) into which rhesus monkey blood had been introduced. It was found that about 85 per cent. of the human white population gave positive reactions to this anti-Rh serum owing to their possessing the appropriate antigen (Rh+). The remaining 15 per cent. gave negative reactions (Rh–).

If a woman who is Rh– is immunized against Rh+ blood she may suffer her-self and she may cause damage to her offspring. This may occur in one of two ways:—(1) She may be transfused with blood which appears to be compatible as judged by the ordinary ABO mechanism. If this blood is Rh+ she does not suffer at the first transfusion, but if on a subsequent occasion she is again given Rh+ blood she may suffer a severe and even fatal reaction. (2) If married to a man whose blood is Rh+ some or all of the offspring, depending upon some genetic considera-tions to be discussed later, may be Rh +, and during pregnancy some of the fœtal blood may escape from the placental villi and cause iso-immunization with the production in the mother's blood of an anti-Rh agglutinin. This agglutinin may pass back into the fœtal circulation and cause damage to the fœtal blood system, resulting in abortion, prematurity, still-birth or hydrops fœtalis. If born alive the child may exhibit hæmolytic anæmia with or without icterus gravis neonatorm. In its severe form death may occur within a short interval after birth. In some cases the child may appear quite healthy at the time of birth, the manifestations first appearing after some hours or days. At autopsy there is massive evidence of blood formation in such sites as the liver and spleen and the nucleated erythrocytes in the circulat-ing blood are increased in number—erythroblastosis. The prompt administration of Rh– blood will save a proportion of these infants.

In some infants dying of erythroblastosis changes are found in the cerebral and cerebellar cortices, especially in the basal ganglia. These changes are associated with bile staining (kernicterus). It has long been known that a proportion of children surviving after icterus gravis later show evidence of spastic paralysis and mental deficiency. Recent work suggests that an appreciable proportion of mental defectiveness in later life may have a similar origin. (This subject was discussed in a leading article in the *British Medical Journal*, August 11, 1945, p. 188.)

some of the sulphonamides. Unfortunately there is no evidence that penicillin is of value in one type of puerperal sepsis, which is frequent and often fatal and which is resistant to the sulphonamides, that, namely, due to the anaerobic streptococci. This is the type of infection found especially after severe trauma of the pelvic soft tissues during labour. For this class of case there is as yet no proved chemotherapeutic measure.

Pyelitis and pyelonephritis.—Since Kenny and her co-workers (1937) demonstrated that the urine in pyelitis of pregnancy due to the *B. coli* could generally be rendered sterile within four or five days with small doses of sulphanilamide, much work has firmly established the place of this group of drugs in this disease: 1.5 to 3 gm. per day is usually a sufficient dose and the choice lies between sulphanilamide or sulphadiazine. Sulphapyridine should never be used because of its high toxicity, and sulphathiazole has the great disadvantage that it tends especially to produce crystalluria (Douglas, 1943). If results are not obtained with the dosage recommended, resistant strains of the *B. coli* (rarely), or other classes of bacteria, such as *Streptococcus fæcalis* or staphylococci, may be the causative factor. In such cases penicillin may prove useful (Thompson, 1944). So far there is little evidence in the literature on the value of penicillin in pyelitis. In cases which do not respond quickly little can be expected from increased or continued dosage of the sulphonamides and in some cases, especially in the severe anæmia often found in pyelitis, there is considerable risk of toxic reactions.

Venereal disease in pregnancy.—The sulphonamides have revolutionized the treatment of *gonorrhœa* during pregnancy. They are effective in moderate doses, 4 gm. daily for three days, followed by 2 gm. daily for a week. As Sorsby (1943) and others have pointed out, prenatal treatment of the mother and of the infected infant after birth has greatly reduced the incidence of blindness and impaired vision due to ophthalmia neonatorum. Many writers warn, however, that in a certain number of cases the immediate, often dramatic, relief of clinical symptoms may be followed by later recurrence or by a persisting asymptomatic infectiveness. For these reasons periodic re-examination after apparent cure is essential. In some cases, moreover, the gonococcus is resistant to the sulphonamide treatment from the beginning. From America, where more penicillin has been available for general clinical use, come reports of the use of this drug in gonorrhœa.

Thompson (1944), using a total dosage of 150,000 Oxford units, claims 98 per cent. cure with no toxic effects. Equally satisfactory results have been obtained in ophthalmia neonatorum after intramuscular injection (Sievers *et al.*, 1944) or locally (Sorsby, 1945). The latter writer obtained good results with a concentration of 2,500 Oxford Units per c.cm. in cases due to gonococci, staphylococci and the virus associated with inclusion blenorrhœa. The irrigation of the eye is well tolerated and it need not usually be continued for more than six hours. At the British Postgraduate Medical School penicillin (1,000 Oxford units per c.cm.) has replaced sliver nitrate as the prophylactic eye drops for the newborn.

There is some evidence that penicillin may be of value in the treatment of prenatal *syphilis*, and it would seem that the drug when administered to the mother reaches the fœtal circulation in effective concentration (Woltz and Zintel, 1945; Parks, 1945). The dose recommended by Lentz and his co-workers (1944) for the pregnant syphilitic woman is 2,400,000 Oxford units given by intramuscular drip over eight days.

Mastitis.—As breast abscess is generally due to infection with staphylococci it is suited for treatment with penicillin. It is claimed that timely administration of the drug in a dosage of 25,000 Oxford units every three hours for three days, followed by 15,000 units three-hourly for two days, is effective in preventing abscess formation (Hodgkinson and Nelson, 1945).

THE RHESUS FACTOR: ERYTHROBLASTOSIS FŒTALIS

The discovery in 1940 of a hitherto unknown blood agglutinogen by Landsteiner and Wiener has thrown new light on certain diseased states in mother and child. This agglutinogen was called Rh because it was found to be present in the serum of rabbits (or guinea-pigs) into which rhesus monkey blood had been introduced. It was found that about 85 per cent. of the human white population gave positive reactions to this anti-Rh serum owing to their possessing the appropriate antigen (Rh+). The remaining 15 per cent. gave negative reactions (Rh–).

If a woman who is Rh– is immunized against Rh+ blood she may suffer herself and she may cause damage to her offspring. This may occur in one of two ways:—(1) She may be transfused with blood which appears to be compatible as judged by the ordinary ABO mechanism. If this blood is Rh+ she does not suffer at the first transfusion, but if on a subsequent occasion she is again given Rh+ blood she may suffer a severe and even fatal reaction. (2) If married to a man whose blood is Rh+ some or all of the offspring, depending upon some genetic considerations to be discussed later, may be Rh +, and during pregnancy some of the fœtal blood may escape from the placental villi and cause iso-immunization with the production in the mother's blood of an anti-Rh agglutinin. This agglutinin may pass back into the fœtal circulation and cause damage to the fœtal blood system, resulting in abortion, prematurity, still-birth or hydrops fœtalis. If born alive the child may exhibit hæmolytic anæmia with or without icterus gravis neonatorm. In its severe form death may occur within a short interval after birth. In some cases the child may appear quite healthy at the time of birth, the manifestations first appearing after some hours or days. At autopsy there is massive evidence of blood formation in such sites as the liver and spleen and the nucleated erythrocytes in the circulating blood are increased in number—erythroblastosis. The prompt administration of Rh– blood will save a proportion of these infants.

In some infants dying of erythroblastosis changes are found in the cerebral and cerebellar cortices, especially in the basal ganglia. These changes are associated with bile staining (kernicterus). It has long been known that a proportion of children surviving after icterus gravis later show evidence of spastic paralysis and mental deficiency. Recent work suggests that an appreciable proportion of mental defectiveness in later life may have a similar origin. (This subject was discussed in a leading article in the *British Medical Journal*, August 11, 1945, p. 188.)

As 85 per cent. of the population is Rh+ and 15 per cent. Rh– it is clear that a not inconsiderable proportion of marriages present the combination of positive father and negative mother.

In 10 per cent. of all pregnancies an Rh– mother carries an Rh+ child. Despite this, hæmolytic disease occurs only once in 400 of all pregnancies. There are several reasons for this. In the first place the first child of such a marriage escapes. Only after carrying one Rh+ child is the mother sensitized. It may take two or more such pregnancies to work the harm; once an erythroblastotic child has been born every subsequent Rh+ child will suffer. In the second place the risk depends upon the husband: if Rh+ he may carry the Rh gene in both chromosomes concerned, in which case he will belong to the genotype RhRh and all his children will be Rh+. Or he may carry this gene in one chromosome only. In this case he belongs to the genotype Rhrh and only half his children will be Rh+. There are other reasons not well understood for the relative rarity of erythroblastosis, for even when the child is Rh+ and there are anti-Rh agglutinins in the mother's serum, the child may be unaffected. Here there are several possible variables, the degree of permeability of the placenta to the fœtal Rh agglutinogen and the capacity of the mother to produce the appropriate antibody. In respect of this latter consideration, however, there is evidence that the most severe manifestation of the disease (hydrops fœtalis) may be associated with a low titre of maternal blood anti-Rh agglutinin. It is possible that a major factor in determining the incidence of the disease is the amount of Rh antigen which is free in the fœtal body fluids and which is capable of absorbing the antibodies that pass back into the fœtal circulation, and thus of saving the erythrocytes themselves.

It is thus apparent that the risk to an Rh+ child borne of an Rh– mother depends, other circumstances being favourable, upon the degree of immunization of the mother. In general it may be said that one pregnancy involving an Rh+ infant or one transfusion with Rh+ blood may precipitate this risk. In general, also, and with the reservation mentioned above, the serological testing of the mother's blood during pregnancy against Rh+ blood provides evidence of the imminence of the risk to the infant of that pregnancy. The presence of anti-Rh agglutinins in the maternal blood is evidence of the phenomenon, and the higher the titre the greater the risk.

So far the serological basis of hæmolytic disease of the fœtus is fairly straightforward and the statements given above apply to over 90 per cent. of cases of the disease. In these 90 per cent. of cases the mother is Rh– and the fathers and infants are Rh+. This observation forms the scientific evidence for the correlation between the Rh factor and the condition because, as already noted, in a random sample of the population only 15 per cent. prove to be Rh–.

In this place only a short reference can be made to the 10 per cent. of cases in which the hæmolytic disease occurs in a child born of a Rh+ mother.

Here a similar process is at work; the mother is immunized by an antigen present in the fœtus but which she does not possess. Sometimes it is one of the Rh subtypes, of which a confusing number have been described. Sometimes it is the Hr factor, whilst in a very few instances it may be the ordinary A or B agglutinogen.

PRACTICAL CONCLUSIONS AND TREATMENT

The mother.—If at any time a woman known to be Rh– and to have

given birth to an Rh+ child requires a blood transfusion, this must always be with Rh– blood. The same applies to a woman whose Rh grouping is not known but who has given birth to an erythroblastotic baby or to a child in whom any suspicion of hæmolytic disease has arisen. It has, indeed, been recommended that, as it is often impossible in the case of an emergency requiring transfusion to obtain satisfactory clinical or serological data, no woman should ever receive Rh+ blood. If she happens to be Rh– and has carried an Rh+ child she may be already sensitized by this pregnancy. Or if she happens to be Rh– she may be sensitized by the transfusion of Rh+ blood with danger to any subsequent pregnancy with an Rh+ child. The same considerations apply when the woman has received a previous transfusion. It has been pointed out that every recorded case of severe hæmolytic reactions following first transfusions had occurred in postpartum women (Wiener and Peters, 1940). When, as must occasionally happen, there is no Rh– blood of the appropriate ABO group available, plasma or serum only should be used for the transfusion.

The infant.—The infant suffering from erythroblastosis, or an infant born to a woman who has lost previous children from this disease, must receive repeated transfusions with Rh– Group O blood begun immediately after birth. To begin with, 100 c.cm. may be immediately introduced into the umbilical vein. The infant, although Rh+, must be given Rh– blood because of the maternal antibodies which are in the fœtal circulation. These antibodies may persist for a considerable time, even months, during which time the treatment may require to be continued. In the absence of Rh– blood the maternal blood cells washed free of the plasma with its antibodies may be used.

In some maternity services all women have their blood tested for the Rh factor during pregnancy with a similar check on the husband when the mother is found to be Rh–. In this way it is hoped that information of value will be obtained for the better management of a condition in which the prognosis is at present still grave. From what has been stated on page 251 it is clear that whenever there is a history of previous unexplained still-births or of frank erythroblastosis in the obstetric history, the pregnant woman should be referred to an institution where the necessary investigations and, in case of need, the appropriate treatment can be carried out.

THE TREATMENT OF PLACENTA PRÆVIA

In the recent literature there are signs of a movement away from the traditional treatment of placenta prævia by immediate termination of the pregnancy. It has generally been taught that when a patient bleeds during the last months of pregnancy a diagnosis should be made at the earliest possible moment, by digital exploration generally, and that when placenta prævia is established the pregnancy must be terminated to safeguard the mother

As 85 per cent. of the population is Rh+ and 15 per cent. Rh– it is clear that a not inconsiderable proportion of marriages present the combination of positive father and negative mother.

In 10 per cent. of all pregnancies an Rh– mother carries an Rh+ child. Despite this, hæmolytic disease occurs only once in 400 of all pregnancies. There are several reasons for this. In the first place the first child of such a marriage escapes. Only after carrying one Rh+ child is the mother sensitized. It may take two or more such pregnancies to work the harm; once an erythroblastotic child has been born every subsequent Rh+ child will suffer. In the second place the risk depends upon the husband: if Rh+ he may carry the Rh gene in both chromosomes concerned, in which case he will belong to the genotype RhRh and all his children will be Rh+. Or he may carry this gene in one chromosome only. In this case he belongs to the genotype Rhrh and only half his children will be Rh+. There are other reasons not well understood for the relative rarity of erythroblastosis, for even when the child is Rh+ and there are anti-Rh agglutinins in the mother's serum, the child may be unaffected. Here there are several possible variables, the degree of permeability of the placenta to the fœtal Rh agglutinogen and the capacity of the mother to produce the appropriate antibody. In respect of this latter consideration, however, there is evidence that the most severe manifestation of the disease (hydrops fœtalis) may be associated with a low titre of maternal blood anti-Rh agglutinin. It is possible that a major factor in determining the incidence of the disease is the amount of Rh antigen which is free in the fœtal body fluids and which is capable of absorbing the antibodies that pass back into the fœtal circulation, and thus of saving the erythrocytes themselves.

It is thus apparent that the risk to an Rh+ child borne of an Rh– mother depends, other circumstances being favourable, upon the degree of immunization of the mother. In general it may be said that one pregnancy involving an Rh+ infant or one transfusion with Rh+ blood may precipitate this risk. In general, also, and with the reservation mentioned above, the serological testing of the mother's blood during pregnancy against Rh+ blood provides evidence of the imminence of the risk to the infant of that pregnancy. The presence of anti-Rh agglutinins in the maternal blood is evidence of the phenomenon, and the higher the titre the greater the risk.

So far the serological basis of hæmolytic disease of the fœtus is fairly straightforward and the statements given above apply to over 90 per cent. of cases of the disease. In these 90 per cent. of cases the mother is Rh– and the fathers and infants are Rh+. This observation forms the scientific evidence for the correlation between the Rh factor and the condition because, as already noted, in a random sample of the population only 15 per cent. prove to be Rh–.

In this place only a short reference can be made to the 10 per cent. of cases in which the hæmolytic disease occurs in a child born of a Rh+ mother.

Here a similar process is at work; the mother is immunized by an antigen present in the fœtus but which she does not possess. Sometimes it is one of the Rh subtypes, of which a confusing number have been described. Sometimes it is the Hr factor, whilst in a very few instances it may be the ordinary A or B agglutinogen.

PRACTICAL CONCLUSIONS AND TREATMENT

The mother.—If at any time a woman known to be Rh– and to have

INVERSION OF THE UTERUS

A simple and effective method for the reposition of puerperal inversion of the uterus has been described by O'Sullivan (1945).

The method consists of distension of the vagina with fluid introduced from a douche-can held 2 or 3 feet above the level of the vagina. The vaginal outlet is blocked by the assistant's hands and, as the intravaginal hydraulic pressure increases, the uterus is gently forced back into its normal position. Replacement of the uterus immediately after the occurrence of the inversion should be aimed at; this prevents the development of shock. If the uterus is outside the vulva it is cleansed by a dettol solution, dusted with sulphanilamide powder, and pushed gently back into the vagina, after which the hydraulic distension is carried out. If the condition is not recognized until severe shock has developed, the cleansing and gentle vaginal reposition is carried out and anti-shock measures are instituted. When the shock is controlled the hydraulic reposition is proceeded with. It is an advantage to tilt up the end of the bed or table before the reposition.

A number of reports by other observers have appeared since the publication of O'Sullivan's paper, bearing witness to the value of this simple method.

References

Burke, B. S., Harding, V.V., and Stuart, H. C. (1943): *J. Pediat.*, **23**, 506.
Colebrook, L. (1946): *J. Obst. Gynæc.*, **53**, 114.
Douglas, G. R. (1943): *Conn. State med. J.*, **7**, 388.
Ebbs, J. H., Tisdall, F. F., and Scott, W. A. (1941): *J. Nutrit.*, **22**, 515.
Hill, A. M. (1944): *Med. J. Austrl.*, **2**, 425.
Hodgkinson, C. P., and Nelson, R. E. (1945): *J. Amer. med. Ass.*, **129**, 269.
Hudson, G. S., and Rucker, M. P. (1945): *Amer. J. Obst. Gynec.*, **50**, 452.
James, J. R. E. (1945): *J. Obst. Gynæc.*, **52**, 501.
Kenny, M. (1945): *Ibid.*, 373.
——, Johnston, F. D., and Von Haebler, T. (1937): *Lancet*, ii, 119.
Landsteiner, K., and Wiener, A. S. (1940): *Proc. Soc. exp. Biol. Med.*, **43**, 223.
Lentz, J. W., Ingraham, N. R., Beerman, H., and Stokes, J. H. (1944): *J. Amer. med. Ass.*, **126**, 408.
Macafee, C. G. H. (1945): *J. Obst. Gynec.*, **52**, 313.
Mackie, M. (1944): *Med. J. Austrl.*, **2**, 428.
O'Sullivan, J. V. (1945): *Brit. med. J.*, ii, 282.
Parks, J. (1945): *Amer. J. Obst. Gynec.*, **50**, 663.
People's League of Health Investigation (1942): *Lancet*, ii, 10.
Sievers, J. J., Knott, L. W., and Soloway, H. M. (1944): *J. Amer. med. Ass.*, **125**, 690.
Sorsby, A. (1943): *Lancet*, ii, 645.
—— (1945): *Brit. med. J.*, i, 114.
Thompson, G. T. (1944): *J. Amer. med. Ass.*, **126**, 403.
Wiener, A. S., and Peters, H. R. (1940): *Ann. int. Med.*, **13**, 2306.
Williams, P. F. (1945): *J. Amer. med. Ass.*, **127**, 1052.
Woltz, J. H. E., and Zintel, H. A. (1945): *Amer. J. Obst. Gynec.*, **50**, 338.

against dangerous blood loss. This method was inevitably associated with a high fœtal loss, chiefly from prematurity, the loss in many instances being as high as 60 to 70 per cent. Macafee (1945) has shown, however, that "expectant" treatment can save many infants without adding to the maternal risk. He reports 174 consecutive cases with one maternal death (0.57 per cent.) and forty-one fœtal deaths (23.5 per cent.). It has always been recognized that women with bleeding during the last months should be admitted immediately to hospital, generally by ambulance, and that, to avoid further detachment of the placenta, they should not be examined vaginally beforehand. Macafee has shown that, after removal to hospital and so long as they are under supervision, in a considerable number of such women the pregnancy can be safely allowed to continue until the child is viable. With increasing recourse to expectancy during the period under review, Macafee has effected a marked saving in infant life.

In his first forty-seven cases the average birth weight of the infant was 5 lb. 2oz. and the mortality 47 per cent., whilst in his last forty-seven cases the average birth weight was 6 lb. 12 oz. and the infant mortality 6 per cent. In one case the patient remained fourteen weeks in hospital before delivery. In every case the final obstetrical examination (apart from gentle exploration with a speculum, if necessary, to exclude a polypus) or interference is carried out in the operating theatre. This allows of the appropriate treatment (rupture of the membranes, application of Willett's forceps, Cæsarean section) being conducted under safe conditions.

The disadvantages of this method are twofold. In the first place it increases the demand for hospital bed provision at a time of great stringency. In the second place it means that, when the source of the bleeding remains in doubt, many cases of accidental hæmorrhage, in which expectant treatment has no proved advantage, are necessarily subjected to the same treatment. I am satisfied that a greater recourse to expectancy in placenta prævia under the conditions laid down above is justified.

At the British Postgraduate Medical School the infant mortality in 108 cases was 19.4 per cent. During the first six years the infant mortality was 29.2 per cent., whereas during the last five years with increasing expectancy it fell to 13.4 per cent. On the other hand, during the same period the infant mortality in a total of 162 cases of accidental hæmorrhage was 32.7 per cent. Expectancy in forty-three cases did not appreciably reduce the mortality (30.2 per cent.).

INDUCTION OF LABOUR

The advantages of rupture of the membranes over the rectal tube for the induction of labour are pointed out in communications by Hill (1944) and Mackie (1944). After rupture of the membranes the onset of labour is quicker and the maternal and fœtal morbidity and mortality are less. With the rectal tube there is at the end of twenty-four hours 100 per cent. bacterial invasion of the uterus; this gravely prejudices the situation in regard to subsequent operative delivery and explains the relatively high morbidity from sepsis after spontaneous delivery.

they do. The use of cubicles is helpful but will not replace strict nursing care. There is much to be said in favour of sick children being nursed separately by their own mothers, as in the plan adopted by Pickerill and Pickerill (1945).

In regard to *air-borne infections*, e.g., the common cold, tonsillitis, otitis media, tracheo-bronchitis, rheumatism, and the frequent complications of measles (Wright, 1945), influenza and whooping-cough, it is now believed that infected dust on floors and bed linen is more dangerous than direct droplet infection. The oiling of floors and bed linen and attempts to sterilize air by ultra-violet irradiation and bactericidal vapours, particularly various glycols, are in use and in some cases excellent results have been claimed. In an attempt to prevent any undesirable effects of permeating the atmosphere with germicidal substances, Danforth, Rudig and Fishbein (1946) have devised a small box-like cabinet into which a fan draws the air of the room through two inlets at the rate of about 220 cubic feet per minute, driving the incoming air downward against the surface of a bactericidal (aqueous) solution containing 2.5 per cent. sodium hydroxide and 1.2 per cent. potassium mercuric iodide. Their experiments with this apparatus have given encouraging results.

Diphtheria and whooping-cough.—The campaign to immunize all children against diphtheria is bearing fruit, but many parents are apathetic and there are still some three million uninoculated children in the country. Doctors should take every opportunity to educate the lay public regarding this method of controlling a dangerous disease. Modern opinion is in favour of giving the first course of immunization (e.g. two doses of A.P.T. separated by a three to four weeks' interval) when the child is six to nine months old, with a "boosting" dose three to five years after the primary course.

Whooping-cough is the most serious of the acute specific fevers in childhood, causing much illness and between two and three thousand deaths annually in this country; and most of these deaths are in children under five years of age. Although the evidence in favour of immunization against whooping-cough is less definite than for diphtheria, a good case can be made for its use, and it is undoubtedly harmless. The total dose recommended is 100,000 million for Sauer's vaccine, or 30,000 to 40,000 million for alum precipitated vaccine; it is given intramuscularly in two or three injections at intervals of three to four weeks.

There is much to be said in favour of combining immunization against diphtheria and whooping-cough, provided that the latter vaccine is not a phenolized preparation, and opinions are now being expressed that infants should receive their injections as early as three to six months of age.

PENICILLIN

General infections.—The optimum dosage for systemic treatment will depend upon various factors, e.g. type of organism, clinical variety of

ADVANCES IN PÆDIATRICS

By NORMAN B. CAPON, M.D., F.R.C.P.

Professor of Child Health, University of Liverpool; Physician, Royal Liverpool Children's Hospital; Visiting Physician, Alder Hey Children's Hospital.

PLANS to improve the pædiatric service are taking shape and they promise to give practical expression to ideals which have long been held, not only by pædiatricians, but by all who are concerned with the welfare of children. Stated in the simplest terms the task consists in finding the most practical answer to the question "How can optimum health be assured and maintained in childhood?". Emphasis is upon prophylaxis, but a complete and comprehensive service must cover all aspects of health and disease. The wide range of pædiatric needs has been described by Craig (1946) in a valuable study which should be read by all who have a part to play in the pædiatric service. It serves to underline Park's (1946) recent statement:— "The advances in medicine have far outstripped their social applications and have created new needs and possibilities."

To secure what is required in the best interests of children there must be better education of parents, medical students, doctors, and nurses; improvement of the environmental conditions (including diet) under which the child lives; a well-planned hospital service; and a coordinated scheme by which practical advice and assistance will be available when needed for each child in his home, at school, or wherever he may be. This is a tremendous task, demanding statesmanship, enthusiasm, patience and, above all, a spirit of understanding and cooperation between the various workers in the pædiatric field. Such a spirit has been evident for some years and its continued growth and intelligent expansion marks the most important of recent advances.

THE PREVENTION AND CONTROL OF INFECTION

Much attention continues to be devoted to this subject, for the spread of contagion is always a menace to children, particularly when they are grouped in communities, e.g., in hospital wards, nurseries and schools. Practical details of much value are to be found in War Memorandum No. 11 of the Medical Research Council (1944) and in the report of the Sub-Committee of the British Pædiatric Association (1946) entitled "Cross Infection in Children's Wards". Special problems confronting pædiatricians working in maternity hospitals have been dealt with by Corner (1946), who has given a detailed report upon the nursing care of the newly born.

Infections transmitted from child to child on the hands of attendants and on napkins, bed linen, and the like, can be prevented when the nursing staff is sufficiently numerous to enable them to do their work without undue hurry and when they are well trained and understand the reasons for what

have reported good results. Sandes (1946) states that the osseous lesions of congenital syphilis respond rapidly to penicillin, but she recommends that arsenic with bismuth or mercury therapy be continued for some time subsequently. In florid cases under twelve months of age the dose recommended is 20,000 units intramuscularly, three-hourly day and night (omitting one night dose to allow more sleep), until a total dose of half a million units has been given. But she warns· that the treatment may be dangerous if given to an acutely ill baby. The dosage used by Heyman and Yampolsky (1946) is at least 200,000 units per kgm. of body weight, given intramuscularly in equally divided doses every three hours, for a period of ten days.

SUBDURAL HÆMATOMA

During recent years it has been shown that the accumulation of a "pocket" of blood between the dura and arachnoid membranes (subdural hæmatoma) is not uncommon in infancy, especially during the first six months of life. The usual anatomical site is the fronto-parietal region, and the hæmatoma may be unilateral or bilateral. Trauma, during or after birth, is the common cause, but there may be no history of injury; even slight trauma seems to be responsible in some cases, especially if the infant has a relative deficiency of vitamin C or vitamin K, or is suffering from purpura, leukæmia, hæmophilia, syphilis or malnutrition. Formerly the condition was seldom suspected clinically except when the child had convulsions accompanied by a gradual enlargement of the head. It is, however, now accepted (Eley, 1945) that these are late manifestations. Early diagnosis is important because vascularization of the clot begins two or three weeks after the bleeding occurs and it then becomes increasingly difficult to drain the hæmorrhage successfully. The early symptoms include pyrexia, vomiting, irritability, excessive crying, neck resistance, and generalized muscular hypertonicity. In some cases the baby is apathetic, refusing to suck satisfactorily and not gaining weight. There is usually increased tension of the anterior fontanelle and a gradual increase of the head circumference. More definite evidence of an intracranial lesion, e.g. convulsions, paralysis of upper motor neurone type, downward displacement of eyes, retinal hæmorrhages and a "cracked-pot" sound on percussion of the skull, may develop.

Puncture of the subdural space is necessary to establish the diagnosis; it can be performed with safety if the technique described by Ingraham and Matson (1944) is followed, and sometimes effective drainage of the hæmatoma is possible in this way by withdrawing 10 to 15 c.cm. at each tapping. A clot which has become vascularized can be removed only after the skull has been trephined. Ingraham and Matson believe that in these cases radical craniotomy with excision or wide decompression of constricting subdural membranes is essential if the child's mental development

infection, age and state of patient. Bodian's (1946) recommendation, which may be accepted as a valuable working basis for infancy, is 1,000 units per pound of "expected" body weight every twenty-four hours; it is divided into six doses, each made up in 1 c.cm. of normal saline and given four-hourly by the intramuscular route. This report was based upon the treatment of 78 infants under the age of one year, and the infections were mainly due to staphylococcus, hæmolytic streptococcus and pneumococcus.

Acute osteomyelitis.—Aird (1945) states that the standard treatment of acute osteomyelitis should include (1) needling of the metaphyseal focus for bacterial diagnosis, sensitivity tests and relief of tension; (2) continuous (distant) intramuscular penicillin instillation maintained until the marrow is sterile; (3) immobilization; and (4) the simple drainage of subcutaneous abscesses. He is satisfied that the value of penicillin in the acute septicæmic form of osteomyelitis appears to be proved. Agerholm and Trueta (1946) suggest that the dosage of systemic penicillin should be 400,000 units in twenty-four hours until the infection appears to be adequately controlled: then 100,000 units in twenty-four hours

Eye infections.—According to Sorsby (1946) about 25 per cent. of cases of ophthalmia neonatorum are due to the gonococcus; staphylococcal infection accounts for about 35 per cent. Both these infections respond well to sulphonamide treatment but even more rapidly to penicillin (2,500 units per c.cm.) instilled into the eye at the rate of one drop each minute. The infection is usually under good control within thirty minutes, although œdema and hyperæmia take longer to subside.

Respiratory infections.—In acute respiratory infections, and in some cases of chronic respiratory infection, such as bronchiectasis, penicillin by inhalation may be a useful adjunct to other treatments. Knott and Southwell (1946) have described a simple method for the administration of penicillin aerosol in an oxygen tent. It is thought that penicillin lozenges or pastilles (500 units in an agar base) are helpful in the treatment of Vincent's angina and catarrhal tonsillitis, and before and after tonsillectomy.

Pneumococcal meningitis.—An illness such as this, almost invariably fatal in the past, constitutes a real challenge to modern technique. By early diagnosis, which must include examination of the cerebrospinal fluid, and by the combined use of a sulphonamide with penicillin, it is now possible to give a better prognosis than formerly, although the mortality and morbidity rates are still high. Hartmann and his co-workers (1945) recommend 20,000 units of penicillin intrathecally, and 10,000 to 20,000 units intramuscularly or subcutaneously, with 0.1 gm. of sulphadiazine per kgm. of body weight every eight or twelve hours subcutaneously. Penicillin injections are continued subcutaneously every two hours, and 10,000 to 20,000 units are injected into the subarachnoid space. Specific serum therapy may also be helpful. The treatment may be required for ten to fourteen days.

Congenital syphilis.—American writers referred to by Marshall (1946)

FUNCTIONAL DISTURBANCES

Attention should be drawn to a potentially harmful effect of child health propaganda. Intelligent and conscientious mothers who read and hear so much regarding the importance of maintaining full health in childhood sometimes become morbidly anxious about their children and are not prepared to take even slight risks, with the result that their children are denied nature's method of learning "by trial and error". For instance, if a young infant refuses part of a meal it is well that he should not be forced to take it; he will probably be hungry by the next day. In some cases, when undue persuasion is used meal after meal, the child is denied the pleasure of satisfying hunger, for he never has an appetite; he then develops indigestion, and maybe anorexia nervosa. This causes much unhappiness both to the parents and to the child; the home becomes a focus of worry. Doctors, nurses, health visitors and others whose advice is sought must be careful that they do not inadvertently fan the flame of parental anxiety. There are many cases of anorexia, constipation and sleeplessness which have been induced by over-solicitation on the part of parents and other adults, and the rapidity of habit formation in childhood complicates the difficulties of treatment. It is by sensible advice and reassurance given in the early stages that such difficulties can be prevented and, whenever possible, such advice should be given personally to the mother rather than by the less personal written word.

PROTEIN DEPLETION

Deficiency of protein and disorders of protein metabolism are frequent in childhood. Loss of appetite, infantile gastro-enteritis and all diseases which are accompanied by wasting (e.g. fibrocystic disease of the pancreas and cœliac disease) may interfere with the ingestion of sufficient protein and may be responsible for ineffective digestion and absorption of such protein as the child can be persuaded to swallow. When the liver is damaged, as in various types of toxic hepatitis and in chronic suppurative conditions, the child's need for amino-acids may be considerable. Oedematous nephritis and the effects of hæmorrhage are other abnormal states which may be helped by giving suitable proteins to replace loss.

In all these conditions, protein digests or hydrolysates may be valuable. They are prepared from milk protein (casein) by the action of acids or enzymes and are available (e.g. "casydrol", "pronutrin") for use by mouth or by injection. The question of dosage is still being investigated; when given by mouth to infants up to one year of age, a suitable amount would appear to be about 0.5 to 1.5 gm. per pound of "expected" body weight. It is administered in a 5 to 10 per cent. solution in cold or iced water, and not more than one day's supply should be prepared at one time. The makers of "casydrol" recommend that it be administered with a suitable proportion (about three times its weight) of glucose fortified with nicotinamide and

is to be safeguarded, for the rapid increase in brain volume during the first two years of life will be restricted by the presence of a clot. If this view is correct it underlines the importance of early diagnosis in order that the simpler methods of treatment may be employed.

CEREBRAL PALSY

Phelps (1943) has shown how much can be done for victims of this cruel disorder. There must be, to quote the words of Evans (1946), "a wide and comprehensive approach from all angles and treatment must be individual, intensive and progressive". Carshalton has set an excellent example in the work of its "Cerebral Palsy Unit", and similar clinics or remedial schools are needed all over the country.

The mental state of the patient must be assessed and after a careful survey of both the mental and the physical condition the child's economic potentiality may be estimated and he may be trained to be independent or at least semi-independent. The best results can be obtained only if there is coordination of effort between doctor, physiotherapist, occupational therapist, speech therapist, school teacher and psychologist. Prostigmin is now in use to lessen spasticity and thus to allow better function of the muscles involved. It is a parasympathetic stimulant which has recently been shown to have a depressant action on the spinal cord; deep reflexes can be abolished and muscle spasm is thereby reduced. The younger the patient, the more effective is the action of this drug. Jepson (1946) reports most encouraging results using 5 mgm. of prostigmin bromide by mouth three, four or more times daily; and both Kabat (1944) and Schaubel (1944) have also recorded success with this treatment. It should be emphasized that physiotherapeutic measures and re-education must be employed concomitantly.

DISORDERS OF THE SPECIAL SENSES

The serious effects of disorders of the special senses in childhood cannot be over-emphasized. When, for instance, vision or hearing is not perfect the child is denied full opportunities of development, both mental and physical: his life is stunted in attainment and he cannot be as happy as the normal child. The pioneer work of the Ewings in Manchester has brought into prominence the value of special methods of testing the hearing of even young children, and has demonstrated the value of careful treatment in the development of both hearing and speech in such cases. Some children are found to have "islets of deafness" which are difficult to recognize; but until this is done they may be regarded as inattentive, lacking in power of concentration, and perhaps mentally backward. It is not surprising that in such children speech may be imperfect and psychological disturbances may develop.

ADVANCES IN ENDOCRINOLOGY

By E. C. DODDS, M.V.O., M.D., F.R.C.P., F.R.S.

From the Courtauld Institute of Biochemistry, Middlesex Hospital.

THE most recent developments in endocrinology as applied to treatment have been the use of thiourea and related compounds in the treatment of thyrotoxicosis, and the use of synthetic œstrogens in the treatment of malignant disease.

THE TREATMENT OF THYROTOXICOSIS

It was observed (Mackenzie and Mackenzie, 1943; Astwood *et al.*, 1943) that the changes produced in the thyroid glands of rats by the administration of certain sulphonamides and thioureas were due to the inhibition of thyroid hormone production. Hyperplasia of the gland was accompanied by a reduction in the basal metabolic rate and an increase in weight. Astwood (1943) decided to apply this observation to the treatment of thyrotoxicosis. He successfully treated three cases, producing relief of symptoms and a return to normal of the basal metabolic rate and blood cholesterol. In all cases there was a delay of one to two weeks before improvement was noticeable. After this initial period the basal metabolic rate began to fall, but if the drug was discontinued it would rise again. Certain toxic effects, of which the most serious was agranulocytosis, were observed in one case.

Thiourea

$$CS\big\langle{}^{NH_2}_{NH_2}$$

2-Thiouracil

$$HC\big\langle{}^{CO.NH}_{CH.NH}\big\rangle CS$$

This form of treatment has now been used by many workers, either as an alternative to thyroidectomy or as a means of preparing the patients for the operation. Himsworth (1944) reported a series of thirty-three cases observed over periods of ten weeks to ten months. All patients had an initial period of treatment with fairly large doses until a conspicuous improvement was noticed. In all cases the basal metabolic rate and pulse rate were reduced, weight and plasma cholesterol were increased, and symptoms such as sweating, skin flush and nervousness disappeared. There was little, if any, effect on the eye signs or the goitre. After this initial period it was found possible to keep the disease under control with very small doses. If the drug was discontinued in the early stages there was a recurrence of symptoms, but it seemed possible that if dosage were reduced by gradual stages over a long period it might be possible eventually to stop administration altogether.

William and Clute (1945) have reported a series of 152 cases: 59 of these subsequently underwent thyroidectomy for various reasons, but good results were achieved with thiouracil alone, and it was found that the patients who underwent operation were a much less serious risk than those prepared

vitamins B_1, B_2 and C; soups, fruit syrups or peppermint may be used as flavouring agents. When administered intravenously a 5 per cent. solution of protein hydrolysate is employed; for children under six years of age 3 gm. of protein daily per kgm. of body weight is recommended. A dose of carbohydrate, 50 to 100 gm. of glucose, preferably vitaminized, is given by mouth before the injection is started.

In all states of hypoproteinæmia, and especially in œdematous nephritis, intravenous injection of 200 to 300 c.cm. of blood plasma may be helpful.

BREAST MILK BANKS

The diet of young infants, whether healthy or sick, should be the milk of healthy mothers, but a supply is not always available. A few breast milk banks have been started and have proved to be most helpful in the nursing care of babies undergoing treatment in children's hospitals, and for premature and sick infants, both in maternity hospitals and in their own homes. Dynski-Klein (1946) has recently emphasized that every maternity unit may be regarded as an ideal background for the creation of an efficient breast milk service, and she tabulates the advantages as follows: simple daily routine in collection and preparation; no special staff or financial measures are needed; the donors are on the spot; medical control is easy; adulteration and contamination of milk are excluded; the supply is continuous and adaptable to the demand and could be extended to out-patients.

References

Agerholm, M., and Trueta, J. (1946): *Lancet*, i, 877.
Aird, I. (1945): *Proc. roy. Soc. Med.*, 38, 569.
Bodian, M. (1946): *Arch. Dis. Child*, 21, 13.
British Pædiatric Association, Sub-Committee on Cross-Infection (1946): *Brit. med. J.*, i, 673.
Corner, B. (1946): *Proc. roy. Soc. Med.*, 39, 383.
Craig, W. S. (1946): " Child and Adolescent Life in Health and Disease ", Edinburgh.
Danforth, T. F., Rudig, D. M., and Fishbein, W. I. (1946): *Mod. Hosp.*, 66, 100.
Dynski-Klein, M. (1946): *Brit. med. J.*, ii, 258.
Eley, R. C. (1945): *Proc. roy. Soc. Med.*, 38, 369.
Evans, E. S. (1946): *Ibid*, 39, 317.
Hartmann, A. F., *et al.* (1945); *J. Pediat*, 27, 115.
Heyman, A., and Yampolsky, J. (1946): *Amer. J. Dis. Child.*, 71, 506.
Ingraham, F. D., and Matson, D. D. (1944): *J. Pediat*, 24, 1.
Jepson, P. N. (1946): *Ibid.*, 28, 65.
Kabat, H. (1944); *Pub. Hlth. Rep.*, 59, 1635.
Knott, F·A·, and Southwell, N. (1946); *Arch. Dis. Child*, 21, 16.
Marshall, J. (1946): *Proc. roy. Soc. Med.*, 39, 465.
Park, E. A. (1946): *J. Pediat*, 28, 106.
Phelps, W. H. (1943): *Clinics*, 2, 981.
Pickerill, H. P., and Pickerill, C. M. (1945): *Brit. med. J.*, i, 159.
Sandes, G. M. (1946): *Proc. roy. Soc. Med.*, 39, 473.
Schaubel, H. J. (1944): *Physiother. Rev.*, 24, 236.
Sorsby, A. (1946): *Proc. roy. Soc. Med.*, 39, 387; *The Practitioner*, 157, 66.
Wright, Joyce (1945): *Brit. med. J.*, i, 285.

ADVANCES IN ENDOCRINOLOGY

By E. C. DODDS, M.V.O., M.D., F.R.C.P., F.R.S.

From the Courtauld Institute of Biochemistry, Middlesex Hospital.

THE most recent developments in endocrinology as applied to treatment have been the use of thiourea and related compounds in the treatment of thyrotoxicosis, and the use of synthetic œstrogens in the treatment of malignant disease.

THE TREATMENT OF THYROTOXICOSIS

It was observed (Mackenzie and Mackenzie, 1943; Astwood *et al.*, 1943) that the changes produced in the thyroid glands of rats by the administration of certain sulphonamides and thioureas were due to the inhibition of thyroid hormone production. Hyperplasia of the gland was accompanied by a reduction in the basal metabolic rate and an increase in weight. Astwood (1943) decided to apply this observation to the treatment of thyrotoxicosis. He successfully treated three cases, producing relief of symptoms and a return to normal of the basal metabolic rate and blood cholesterol. In all cases there was a delay of one to two weeks before improvement was noticeable. After this initial period the basal metabolic rate began to fall, but if the drug was discontinued it would rise again. Certain toxic effects, of which the most serious was agranulocytosis, were observed in one case.

This form of treatment has now been used by many workers, either as an alternative to thyroidectomy or as a means of preparing the patients for the operation. Himsworth (1944) reported a series of thirty-three cases observed over periods of ten weeks to ten months. All patients had an initial period of treatment with fairly large doses until a conspicuous improvement was noticed. In all cases the basal metabolic rate and pulse rate were reduced, weight and plasma cholesterol were increased, and symptoms such as sweating, skin flush and nervousness disappeared. There was little, if any, effect on the eye signs or the goitre. After this initial period it was found possible to keep the disease under control with very small doses. If the drug was discontinued in the early stages there was a recurrence of symptoms, but it seemed possible that if dosage were reduced by gradual stages over a long period it might be possible eventually to stop administration altogether.

Williams and Clute (1945) have reported a series of 152 cases: 59 of these subsequently underwent thyroidectomy for various reasons, but good results were achieved with thiouracil alone, and it was found that the patients who underwent operation were a much less serious risk than those prepared

vitamins B_1, B_2 and C; soups, fruit syrups or peppermint may be used as flavouring agents. When administered intravenously a 5 per cent. solution of protein hydrolysate is employed; for children under six years of age 3 gm. of protein daily per kgm. of body weight is recommended. A dose of carbohydrate, 50 to 100 gm. of glucose, preferably vitaminized, is given by mouth before the injection is started.

In all states of hypoproteinæmia, and especially in œdematous nephritis, intravenous injection of 200 to 300 c.cm. of blood plasma may be helpful.

BREAST MILK BANKS

The diet of young infants, whether healthy or sick, should be the milk of healthy mothers, but a supply is not always available. A few breast milk banks have been started and have proved to be most helpful in the nursing care of babies undergoing treatment in children's hospitals, and for premature and sick infants, both in maternity hospitals and in their own homes. Dynski-Klein (1946) has recently emphasized that every maternity unit may be regarded as an ideal background for the creation of an efficient breast milk service, and she tabulates the advantages as follows: simple daily routine in collection and preparation; no special staff or financial measures are needed; the donors are on the spot; medical control is easy; adulteration and contamination of milk are excluded; the supply is continuous and adaptable to the demand and could be extended to out-patients.

References

Agerholm, M., and Trueta, J. (1946): *Lancet*, i, 877.
Aird, I. (1945): *Proc. roy. Soc. Med.*, **38**, 569.
Bodian, M. (1946): *Arch. Dis. Child*, **21**, 13.
British Pædiatric Association, Sub-Committee on Cross-Infection (1946): *Brit. med. J.*, i, 673.
Corner, B. (1946): *Proc. roy. Soc. Med.*, **39**, 383.
Craig, W. S. (1946): " Child and Adolescent Life in Health and Disease ", Edinburgh.
Danforth, T. F., Rudig, D. M., and Fishbein, W. I. (1946): *Mod. Hosp.*, **66**, 100.
Dynski-Klein, M. (1946): *Brit. med. J.*, ii, 258.
Eley, R. C. (1945): *Proc. roy. Soc. Med.*, **38**, 369.
Evans, E. S. (1946): *Ibid*, **39**, 317.
Hartmann, A. F., *et al.* (1945); *J. Pediat*, **27**, 115.
Heyman, A., and Yampolsky, J. (1946): *Amer. J. Dis. Child.*, **71**, 506.
Ingraham, F. D., and Matson, D. D. (1944): *J. Pediat*, **24**, 1.
Jepson, P. N. (1946): *Ibid.*, **28**, 65.
Kabat, H. (1944); *Pub. Hlth. Rep.*, **59**, 1635.
Knott, F·A·, and Southwell, N. (1946); *Arch. Dis. Child*, **21**, 16.
Marshall, J. (1946): *Proc. roy. Soc. Med.*, **39**, 465.
Park, E. A. (1946): *J. Pediat*, **28**, 106.
Phelps, W. H. (1943): *Clinics*, **2**, 981.
Pickerill, H. P., and Pickerill, C. M. (1945): *Brit. med. J.*, i, 159.
Sandes, G. M. (1946): *Proc. roy. Soc. Med.*, **39**, 473.
Schaubel, H. J. (1944): *Physiother. Rev.*, **24**, 236.
Sorsby, A. (1946): *Proc. roy. Soc. Med.*, **39**, 387; *The Practitioner*, **157**, 66.
Wright, Joyce (1945): *Brit. med. J.*, i, 285.

patients, five are still alive, four with no signs of malignancy; the fifth has a slowly growing tumour but is apparently otherwise in good health. In only three patients was there no remission of symptoms at all, and one of these died of pneumonia eight days after treatment had started. Of the thirteen other patients, four had complications which hastened their end and all thirteen obtained some benefit lasting from five months to four-and-a-half years. Huggins compares these results with the series of untreated cases reviewed by Bumpus (1926) and with various other series of cases treated by other methods. There is no doubt that anti-androgenic measures have produced the best results so far known and, of all the methods which offer, it would seem that the administration by mouth of synthetic œstrogens is the method which produces the least pain, discomfort and inconvenience to the patient.

Results of a similar nature to those of Huggins have been obtained in this country. Although the series of patients does not go back for quite so long a time, an analysis of the results has shown that, whereas practically all cases respond in the first instance, there is, as Huggins points out, a gradual escape from control in a certain percentage. The treatment of such refractory patients has proved to be very difficult. Changing the type of œstrogen or increasing the dose appears to have no effect. At present there is no adequate explanation of this phenomenon, but it may be that androgen is being secreted from tissues other than the testis. The mind naturally turns to the suprarenal cortex, and in support of this explanation is the accepted fact that the suprarenal cortex is not dominated by the anterior lobe of the pituitary as are the gonads. Huggins and Scott (1945) have recently described the effect of adrenalectomy on patients with recurrent symptoms after castration. Whilst it is too early to give any opinion as to the value of such treatment, the results were not of a dramatic or striking character.

A recent publication by Cox (1946) reviews the results of treating a series of cases of carcinoma of the prostate by various operative procedures combined with the administration of synthetic œstrogens. This author maintains that the relief of retention due to prostatic obstruction is not always achieved by stilbœstrol, and that perurethral resection is the method of choice. He also emphasizes the need for large doses, recommending 30 mgm. of stilbœstrol per day. He favours dienœstrol, but in my opinion, in view of the doubtful potency of dienœstrol as compared with stilbœstrol in the human subject, great caution should be observed before a change from stilbœstrol to dienœstrol is made. Last year I gave a review of the experience in this country, together with a report of a typical case (Dodds, 1945).

THE TREATMENT OF CARCINOMA OF THE BREAST

It was only natural that success in the treatment of carcinoma of the prostate with synthetic œstrogens should lead to an attempt at control of other forms

with iodine alone, although the thyroid gland tended to be more friable and to ooze more.

All workers emphasize the importance of careful observations for toxic reactions. The most serious ones reported are agranulocytosis and leucopenia, and various skin reactions have also been reported. It is possible to produce myxœdema with overdosage, and it appears to be considered wiser as a rule to give small doses over a long period rather than to try to produce quick effects with large doses. It is still too early to assess the ultimate value of the treatment or to say whether it should be used as an alternative to, or as a preparation for, thyroidectomy, but it does appear that the drugs are useful in the treatment of thyrotoxicosis, provided the patient is under proper observation.

THE TREATMENT OF CARCINOMA OF THE PROSTATE

The use of œstrogens in carcinoma of the prostate is due to the work of Huggins. By experiments on dogs (Huggins and Clark, 1940) he found that the administration of œstrogens had the same effect on the hyperplastic prostate as castration. In the following year he applied this finding to the treatment of a series of patients with advanced prostatic carcinoma (Huggins et al., 1941a). All these patients underwent orchidectomy and some were given œstrogens as well. Out of twenty-one cases all but three were benefited. The benefits included relief of pain and urinary symptoms and in some cases a decrease in the size of the primary tumour and secondaries. These results have encouraged other workers and there are now many reports of cases treated with œstrogens alone. It appears that the uniformity of response is high. The beneficial effects are shown not only by the relief of pain and urinary symptoms but also by the increased weight and improved appetite of the patients, and the improvement in general condition as shown by blood counts and sedimentation rate. There are now many reports of patients previously bedridden and in acute pain and discomfort who have been enabled to resume their normal activities.

The effects of the treatment are also shown very strikingly in the reduction of the serum level of acid phosphatase. A raised serum level of acid phosphatase has been shown (Gutman, Sproul and Gutman, 1936; Barringer and Woodard, 1938) to be an important diagnostic sign of the presence of carcinoma of the prostate with metastases. This enzyme is present in large quantities in the prostate gland of adult men and its presence has been described by Huggins et al. (1941b) as a secondary sexual characteristic of a chemical nature. The serum level can be reduced by any measure which inhibits the activity of androgens.

Although the majority of patients treated with anti-androgenic measures show some response, in many cases the improvement is not permanent. Huggins (1946) has now published a review of his first twenty-one patients on whom treatment was begun more than five years ago. Of the twenty-one

and Moir (1942) have reported the successful use of triphenylchlorethylene for the inhibition of lactation. Way (1946) and Greene (1946) report the use of DBE for the treatment of menopausal symptoms, and in three cases of uterine atrophy and three cases of carcinoma of the prostate. It was found effective in the treatment of menopausal symptoms. There was a slight response in one case of uterine atrophy. One early case of prostatic carcinoma in which the prostate was enucleated has since been free of symptoms, but the other two cases showed no appreciable response to DBE and responded

Triphenylethylene

α, α, β-Triphenyl-β-chlorethylene

"DBE."
(α, α-*bis*(p-ethoxyphenyl)-β-phenyl-β-bromoethylene
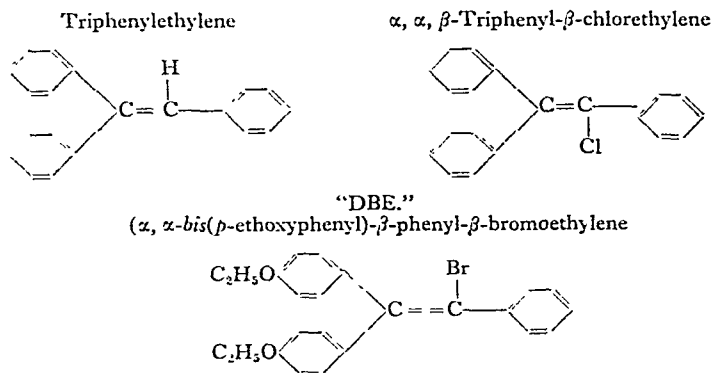
dramatically to stilbœstrol. Only very slight toxic effects were reported by Greene, but Way reports vomiting in four patients, nausea after large doses in three others, uterine bleeding in three patients, severe uterine colic in two and headache in five.

The activity of these compounds is very low compared with that of the stilbœstrol series and very large doses have to be given. It is claimed that a single dose is effective for a long period and this is certainly the case with DBE. This effect is ascribed (Robson and Ansari, 1943) to the fact that, unlike the other œstrogens, it is not inactivated by the liver or rapidly excreted, but that a considerable amount is stored in body tissues, particularly in the fat. It is, however, doubtful whether this prolonged action is an advantage. The great benefit of the stilbœstrol series of compounds is that if it should be necessary to discontinue the œstrogenic action, withdrawal of the treatment is followed by rapid excretion and the effect ceases after twenty-four hours. Methods which give prolonged œstrogenic activity, such as the use of DBE or crystal implantation, make control much more difficult.

Blanchard and his colleagues (1943) prepared a series of *diphenylpropane* derivatives of which the most active has been given the name octofollin. Clinical trials made with this compound (Hufford, 1943; Roberts *et al.*, 1943) show that it can be used for the treatment of menopausal symptoms without untoward effects, but opinions as to dosage required appear to be

of cancer. There has been an outburst of uncritical empiricism by persons who did not realize the sound scientific basis upon which Huggins's work was founded. Out of a large number of letters, articles, and the like, there appears to emerge a fairly definite observation that a very small percentage of cases of carcinoma of the breast are benefited. The Radiological Section of the Royal Society of Medicine (1944) collected over 100 cases treated by the administration of synthetic œstrogens, and the consensus of opinion at that meeting was that not more than 5 per cent. of cases were favourably affected. Again, this is not a quantitative phenomenon; I have tried enormous doses in cases of inoperable carcinoma of the breast without producing any results whatsoever. It is at present impossible to say which cases respond and, if a favourable response is obtained, for how long it will last. It is, however, the opinion of experienced clinicians in this field that the administration of synthetic œstrogens to inoperable cases of carcinoma of the breast is a justifiable empiricism.

SYNTHETIC ŒSTROGENS

So far as the choice of œstrogen goes, the ones in common use are still those of the stilbœstrol series, but other synthetic compounds have since been discovered and some of these have been used clinically.

Stilbœstrol

$$HO-C_6H_4-C(C_2H_5)=C(C_2H_5)-C_6H_4-OH$$

Hexœstrol

$$HO-C_6H_4-CH(C_2H_5)-CH(C_2H_5)-C_6H_4-OH$$

Dienœstrol

$$HO-C_6H_4-C(=CH\cdot CH_3)-C(=CH\cdot CH_3)-C_6H_4-OH$$

Diphenylethylene (stilbene)

$$C_6H_5-CH=CH-C_6H_5$$
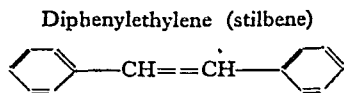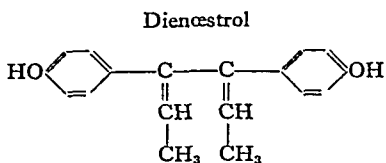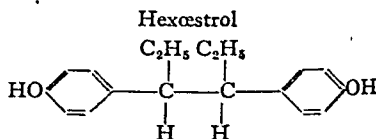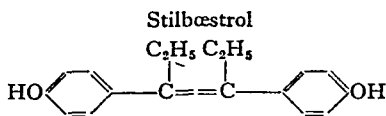
Diphenylethylene (stilbene) was found to possess definite œstrogenic activity (Dodds and Lawson, 1937). Robson and his colleagues (1937, 1938, 1942) prepared and tested triphenylethylene and a number of derivatives. These include *triphenylchlorethylene* and, α,α-*bis*(*p*-ethoxyphenyl)-β-phenyl-β-bromoethylene (called DBE). A few articles have appeared on the clinical trial of these compounds. Macpherson and Robertson (1939) reported the use of triphenylchlorethylene in the treatment of amenorrhœa, vulvitis, vaginitis, menopausal symptoms and for the inhibition of lactation. The compound was given either orally, by injection in oil or in the form of suppositories. It was found possible to administer large doses over a long period of time without ill-effects. When given orally its duration of action was found about equal to that of stilbœstrol, but when given by injection the duration of action was very prolonged. Haultain and Macpherson (1942)

the name of "synapoidin" is made by Parke Davis, and it is claimed that the combination of the two substances has a synergistic effect. It has been used with some success in the treatment of amenorrhœa, functional uterine bleeding and sterility.

On the other hand, Rydberg and Pedersen-Bjergaard (1943) found that the best results were obtained by the administration first of follicle-stimulating gonadotrophin, followed by chorionic gonadotrophin. In this way they produced follicle stimulation followed by the changes in the endometrium which should occur at menstruation.

It is impossible to lay down any hard and fast rules for the treatment of such cases, as each case must be studied individually to find out if possible what is the cause of the abnormality. The preparations are extremely potent and must be used with great caution, frequent examinations being made to guard against untoward effects.

References

Astwood, E. B. (1943): *J. Amer. med. Ass.*, **122**, 78.
——, Sullivan, J., Bissell, Adele, and Tyslowitz, R. (1943): *Endocrinol.*, **32**, 210.
Barringer, B. S., and Woodard, H. Q. (1938): *Trans. Amer. Ass. Genito-Urin. Surg.*, **31**, 363.
Bishop, P. M. F. (1946): " Gynæcological Endocrinology ", Edinburgh, p. 17.
Blanchard, E. W., Stuard, H. A., and Tallman, R. C. (1943): *Endocrinol.*, **32**, 307.
Bumpus, H. C., Jun. (1926): *Surg. Gynec. Obstet*, **43**, 150.
Cox, H. T. (1946): *Brit. med. J.*, ii, 191.
Dodds, E. C. (1945): *West Lond. med. J.*, **50**, 50.
——, and Lawson, W. (1937): *Nature*, **139**, 627.
Greene, R. (1946): *Brit. med. J.*, i, 9.
Gutman, E. B., Sproul, E. E., and Gutman, A. B. (1936): *Amer. J. Cancer*, **28**, 485.
Haultain, W. F. T., and Macpherson, A. I. S. (1942): *Brit. med. J.*, i, 770.
Himsworth, H. P. (1944): *Proc. roy. Soc. Med.*, **37**, 693.
Hufford, A. K. (1943): *J. Amer. med. Ass.*, **123**, 259.
Huggins, C. (1946): *Ibid*, **131**, 576.
——, and Clark, P. J. (1940): *J. exper. Med.*, **72**, 747.
——, and Scott, W. W. (1945): *Ann. Surg.*, **122**, 1031.
——, ——, and Hodges, C. V. (1941a): *J. Urol.*, **46**, 997.
——, Stevens, R. E., Jun., and Hodges, C. V. (1941b): *Arch. Surg.*, **43**, 209.
MacCorquodale, D. W., Levin, L., Thayer, S. A., and Doisy, E. A. (1933): *J. Biol. Chem.*, **101**, 753.
——, Thayer, S. A., and Doisy, E. A. (1933): *Ibid.*, **99**, 327.
Mackenzie, C. G., and Mackenzie, J. B. (1943): *Endocrinol.*, **32**, 185.
Macpherson, A. I. S., and Robertson, E. M. (1939): *Lancet*, ii, 1362.
Miescher, K. (1944): *Helv. Chim. Acta*, **27**, 1727.
Moir, J. C. (1942): *Brit. med. J.*, ii, 681.
Proc. roy. Soc. Med., 1944, **37**, 731.
Roberts, H., Loeffel, Ellen, and MacBryde, C. M. (1943): *J. Amer. med. Ass.*, **123**, 261.
Robson, J. M., and Ansari, M. (1943): *J. Pharmacol.*, **79**, 340.
——, and Schonberg, A. (1937): *Nature*, **140**, 196.
——, —— (1942); *Ibid*, **150**, 22.
——, and Fahim, H. A. (1938): *Ibid*, **142**, 292.
Rydberg, E., and Pedersen-Bjergaard, K. (1943): *J. Amer. med. Ass.*, **121**, 1117.
Way, S. (1946): *Brit. med. J.*, i, 10.
Williams, R. H., and Clute, H. M. (1945): *J. Amer. med. Ass.*, **128**, 65.

conflicting. It seems to be less active, both in the human subject and in animals, than the compounds of the stilbœstrol series.

Octofollin
2, 4-*bis*(*p*-hydroxyphenyl)-3-ethylhexane

HO⟨ ⟩—CH——CH——CH—⟨ ⟩OH
              | | |
             CH₃   C₂H₅   C₂H₅

Equivalent: HO—C₆H₄—CH(CH_3)—CH(C_2H_5)—CH(C_2H_5)—C₆H₄—OH
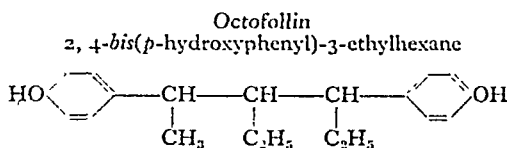
A further group of synthetic œstrogens consists of *doisynolic acid* and its naphthol derivative, *bisdehydrodoisynolic acid*. Doisynolic acid was first obtained in Doisy's laboratory (MacCorquodale, *et al.*, 1933) from œstradiol and, in 1944, Miescher determined its constitution and also prepared by total synthesis *bis*dehydrodoisynolic acid. A very high potency is claimed for both these substances. Oestrus is said to be produced in rats by doses of 0.7 to 1.0γ of doisynolic acid and 0.1 to 0.2γ of *bis*dehydrodoisynolic acid.

Doisynolic acid   *Bis*dehydrodoisynolic acid

         CH₃   CH₃
          |_COOH |_COOH
          ⁻C₂H₅   ⁻C₂H₅

HO   HO
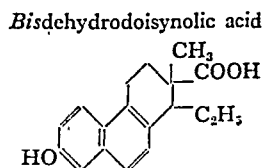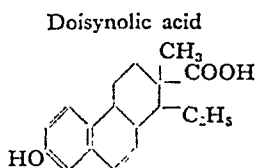
Recent researches have shown, however, that it is unwise to translate results of animal experiments direct to the human subject. There is definite evidence, for instance, that whilst hexœstrol is the most powerful œstrogen when injected subcutaneously in ovariectomized rats, there appears to be little doubt that this same does not apply to the human subject. On purely rough clinical judgement it would appear that stilbœstrol is the most potent, dienœstrol the next and hexœstrol the least potent (Bishop, 1946).

The clinician is constantly searching for synthetic œstrogens active by the oral route in the hope that he will find a substance possessing all the potency of stilbœstrol without the side-reactions, such as nausea, vertigo, and the like, which undoubtedly occur in a small percentage of cases. In my opinion, however, these side-effects are associated with the œstrogenic activity of the substances and cannot be dissociated from it.

GONADOTROPHIC HORMONES

A field which offers opportunities for research is that of the gonadotrophic hormones. So far the constitution of these substances is not known and the only preparations available for use are chorionic gonadotrophin prepared from human pregnancy urine and follicle-stimulating gonadotrophin prepared from pregnant mares' serum or from the anterior lobe of the pituitary gland. Various preparations of these hormones are on the market in a form suitable for intramuscular injection. A mixture of the two under

the name of "synapoidin" is made by Parke Davis, and it is claimed that the combination of the two substances has a synergistic effect. It has been used with some success in the treatment of amenorrhœa, functional uterine bleeding and sterility.

On the other hand, Rydberg and Pedersen-Bjergaard (1943) found that the best results were obtained by the administration first of follicle-stimulating gonadotrophin, followed by chorionic gonadotrophin. In this way they produced follicle stimulation followed by the changes in the endometrium which should occur at menstruation.

It is impossible to lay down any hard and fast rules for the treatment of such cases, as each case must be studied individually to find out if possible what is the cause of the abnormality. The preparations are extremely potent and must be used with great caution, frequent examinations being made to guard against untoward effects.

References

Astwood, E. B. (1943): *J. Amer. med. Ass.*, **122**, 78.
——, Sullivan, J., Bissell, Adele, and Tyslowitz, R. (1943): *Endocrinol.*, **32**, 210.
Barringer, B. S., and Woodard, H. Q. (1938): *Trans. Amer. Ass. Genito-Urin. Surg.*, **31**, 363.
Bishop, P. M. F. (1946): " Gynæcological Endocrinology", Edinburgh, p. 17.
Blanchard, E. W., Stuard, H. A., and Tallman, R. C. (1943): *Endocrinol.*, **32**, 307.
Bumpus, H. C., Jun. (1926): *Surg. Gynec. Obstet*, **43**, 150.
Cox, H. T. (1946): *Brit. med. J.*, ii, 191.
Dodds, E. C. (1945): *West Lond. med. J.*, **50**, 50.
——, and Lawson, W. (1937): *Nature*, **139**, 627.
Greene, R. (1946): *Brit. med. J.*, i, 9.
Gutman, E. B., Sproul, E. E., and Gutman, A. B. (1936): *Amer. J. Cancer*, **28**, 485.
Haultain, W. F. T., and Macpherson, A. I. S. (1942): *Brit. med. J.*, i, 770.
Himsworth, H. P. (1944): *Proc. roy. Soc. Med.*, **37**, 693.
Hufford, A. K. (1943): *J. Amer. med. Ass.*, **123**, 259.
Huggins, C. (1946): *Ibid*, **131**, 576.
——, and Clark, P. J. (1940): *J. exper. Med.*, **72**, 747.
——, and Scott, W. W. (1945): *Ann. Surg.*, **122**, 1031.
——, ——, and Hodges, C. V. (1941a): *J. Urol.*, **46**, 997.
——, Stevens, R. E., Jun., and Hodges, C. V. (1941b): *Arch. Surg.*, **43**, 209.
MacCorquodale, D. W., Levin, L., Thayer, S. A., and Doisy, E. A. (1933): *J. Biol. Chem.*, **101**, 753.
——, Thayer, S. A., and Doisy, E. A. (1933): *Ibid.*, **99**, 327.
Mackenzie, C. G., and Mackenzie, J. B. (1943): *Endocrinol.*, **32**, 185.
Macpherson, A. I. S., and Robertson, E. M. (1939): *Lancet*, ii, 1362.
Miescher, K. (1944): *Helv. Chim. Acta*, **27**, 1727.
Moir, J. C. (1942): *Brit. med. J.*, ii, 681.
Proc. roy. Soc. Med., 1944, **37**, 731.
Roberts, H., Loeffel, Ellen, and MacBryde, C. M. (1943): *J. Amer. med. Ass.*, **123**, 261.
Robson, J. M., and Ansari, M. (1943): *J. Pharmacol.*, **79**, 340.
——, and Schonberg, A. (1937): *Nature*, **140**, 196.
——, —— (1942); *Ibid*, **150**, 22.
——, and Fahim, H. A. (1938): *Ibid*, **142**, 292.
Rydberg, E., and Pedersen-Bjergaard, K. (1943): *J. Amer. med. Ass.*, **121**, 1117.
Way, S. (1946): *Brit. med. J.*, i, 10.
Williams, R. H., and Clute, H. M. (1945): *J. Amer. med. Ass.*, **128**, 65.

ADVANCES IN DERMATOLOGY

By A. C. ROXBURGH, M.D., F.R.C.P.

Emeritus Physician for Diseases of the Skin, St. Bartholomew's Hospital.

·THE greatest advance in treatment in dermatology in the last year or two has undoubtedly been the introduction and increasing availability of penicillin. Penicillin can be used by intramuscular injection, 15,000 to 20,000 units or more in 1 c.cm. of distilled water or saline three-hourly; or by local application as a solution by means of a spray, using 500 to 1,000 units per c.cm. of distilled water, or as a cream, using 400 to 500 units per gramme. Cream bases are available commercially but the perfect base has not yet been found. Many of them contain lanette wax S.X., which is a very useful emulsifier but irritates the skin of some patients. The spraying on of a solution thrice daily is suitable for in-patients but the application of a cream twice daily is more convenient for out-patients and for private use. Whichever preparation is used it should be kept in a refrigerator or at least in a cool place. The solution deteriorates after a week at room temperature but the cream will remain active for about a month. Both should, when possible, be kept in a refrigerator at 5° C. (41° F.).

Penicillin should always be used locally rather than systemically if the disease admits of it, for local use produces a much higher concentration of the drug at the required site than it is possible to obtain by intramuscular injection. When using cream, a sterilized knife blade or spoon must be used to remove the cream from the pot, the lid must be screwed on again at once, and no cream must ever be put back in the pot. In all cases the cream should be applied twice and the spray three times daily.

DISEASES SUITABLE FOR LOCAL APPLICATIONS OF PENICILLIN

Impetigo.—The crusts should be bathed off with normal saline or removed by fomentations or starch poultices. The penicillin should be applied to the whole face to prevent new lesions arising. Impetigo is usually cured in five days. If not cured in a week, penicillin should be replaced by some other antiseptic, e.g., a half per cent. quinoline emulsion.

Bullous impetigo.—The bullæ should be cut away with scissors, so far as possible, and the penicillin preparation applied to the raw surface, being worked well under the remaining edges of the blisters.

Ecthyma.—The crusts must be removed by fomentations or starch poultices and the penicillin applied to the ulcers. A waterproof dressing should then be applied.

Intertrigo.—If this happens to be due to streptococcal infection it will clear up with penicillin: if due to monilia it will not.

Streptococcal fissures usually heal rapidly with penicillin applications. If not healed in seven days other treatment should be adopted.

Otitis externa sometimes improves markedly with penicillin locally as a solution on a wick, but often does not respond owing to the presence of penicillin-resistant organisms.

Blepharitis.—Most cases clear up rapidly on treatment with penicillin cream applied to the edges of the lids night and morning or with penicillin drops put into the conjunctival sac three or four times a day. In a few cases the cream base irritates the conjunctiva. As in all chronic staphylococcal infections, relapse may occur.

Sycosis barbæ.—Penicillin clears up most cases of staphylococcal sycosis very rapidly but they are distressingly liable to relapse. In some cases prolonged use of penicillin cream or spray causes irritation of the skin and in others the staphylococci become penicillin-resistant. In all instances the patient should clip the beard and not shave it while the disease is active, and even when he resumes shaving he should do so with the lie of the beard, not against it. Other possible foci of staphylococcal infection in the nose, sinuses, teeth, tonsils, external auditory meatus, and also seborrhœa of the scalp, must be dealt with.

Impetigo of Bockhart (staphylococcal perifolliculitis of thighs and other hairy areas).—As the infection here is very superficial it often clears up with penicillin applied locally. In obstinate cases penicillin may be used both locally and systemically.

Infective eczematoid dermatitis.—If this is due to a penicillin-sensitive organism it clears up well with penicillin cream or spray; if not, it does not improve.

Skin lesions secondarily infected with penicillin-sensitive organisms.—Such are eczema, seborrhœic dermatitis, sulphonamide dermatitis, radiodermatitis, scabies, lichen urticatus and varicose ulcer. These are usually found greatly improved when the application of penicillin for five to seven days has cleared up the secondary infection. If penicillin-resistant organisms are present in quantity, little improvement will occur.

DISEASES REQUIRING SYSTEMIC PENICILLIN

In these the organisms are out of reach of locally applied penicillin.

Boils and carbuncles.—These are usually cleared up rapidly by six to seven days of penicillin injections, 20,000 units three-hourly, preferably with the local application of penicillin as well. Relapse often occurs, however, a week or two later and the course may have to be repeated.

Erysipelas.—This usually being highly responsive to sulphonamides seldom requires penicillin injections but responds rapidly to 20,000 units three-hourly for five to six days.

Erythema serpens (erysipeloid).—This infection of the skin with *Erysipelothrix rhusiopathiæ* clears up with the injection of 15,000 to 20,000 units three-hourly for four days.

Actinomycosis.—Some cases have been reported cured by five to six

ADVANCES IN DERMATOLOGY

By A. C. ROXBURGH, M.D., F.R.C.P.

Emeritus Physician for Diseases of the Skin, St. Bartholomew's Hospital.

THE greatest advance in treatment in dermatology in the last year or two has undoubtedly been the introduction and increasing availability of penicillin. Penicillin can be used by intramuscular injection, 15,000 to 20,000 units or more in 1 c.cm. of distilled water or saline three-hourly; or by local application as a solution by means of a spray, using 500 to 1,000 units per c.cm. of distilled water, or as a cream, using 400 to 500 units per gramme. Cream bases are available commercially but the perfect base has not yet been found. Many of them contain lanette wax S.X., which is a very useful emulsifier but irritates the skin of some patients. The spraying on of a solution thrice daily is suitable for in-patients but the application of a cream twice daily is more convenient for out-patients and for private use. Whichever preparation is used it should be kept in a refrigerator or at least in a cool place. The solution deteriorates after a week at room temperature but the cream will remain active for about a month. Both should, when possible, be kept in a refrigerator at 5° C. (41° F.).

Penicillin should always be used locally rather than systemically if the disease admits of it, for local use produces a much higher concentration of the drug at the required site than it is possible to obtain by intramuscular injection. When using cream, a sterilized knife blade or spoon must be used to remove the cream from the pot, the lid must be screwed on again at once, and no cream must ever be put back in the pot. In all cases the cream should be applied twice and the spray three times daily.

DISEASES SUITABLE FOR LOCAL APPLICATIONS OF PENICILLIN

Impetigo.—The crusts should be bathed off with normal saline or removed by fomentations or starch poultices. The penicillin should be applied to the whole face to prevent new lesions arising. Impetigo is usually cured in five days. If not cured in a week, penicillin should be replaced by some other antiseptic, e.g., a half per cent. quinoline emulsion.

Bullous impetigo.—The bullæ should be cut away with scissors, so far as possible, and the penicillin preparation applied to the raw surface, being worked well under the remaining edges of the blisters.

Ecthyma.—The crusts must be removed by fomentations or starch poultices and the penicillin applied to the ulcers. A waterproof dressing should then be applied.

Intertrigo.—If this happens to be due to streptococcal infection it will clear up with penicillin: if due to monilia it will not.

Streptococcal fissures usually heal rapidly with penicillin applications. If not healed in seven days other treatment should be adopted.

ARSENICAL DERMATITIS

A compound called B.A.L. (British Anti-Lewisite) was developed in secret during the recent war and proved to be a valuable weapon in the treatment of arsenical dermatitis. It is not yet on the market but the dosage is said to be up to 4 mgm. per kgm. of body weight, given intramuscularly in oily solution at intervals of four hours. It should not be used in cases in which the liver is damaged (*Lancet*, 1945).

CALCIFEROL IN LUPUS VULGARIS

A great step forward in the treatment of lupus vulgaris has been taken by Dowling and Prosser Thomas (1946) in this country and by Charpy (1943) in France. These observers found independently that the administration of calciferol (vitamin D_2), to the extent of 150,000 international units daily by mouth, has a highly beneficial effect on the majority of cases of lupus vulgaris. Dowling and Prosser Thomas gave the calciferol in the form of high potency ostelin tablets (Glaxo) 50,000 units in each, one tablet being swallowed thrice daily. Charpy gave it in solution.

One hundred and fifty thousand units daily is as much as most patients can take without feeling sick and the dose has been reduced after varying periods to 100,000 or 50,000 units daily. Hypercalcæmia occurred in only three cases out of thirty-eight, levels of 12.6, 12.8, and 14.8 mgm. per 100 c.cm. of blood being recorded. These patients did not show any clinical symptoms of intolerance. Evidently clinical symptoms of poisoning are a better guide to the dosage being too high than is the blood calcium level; nausea, loss of appetite, depression or feeling out of sorts are the usual symptoms complained of. Of Dowling's patients, eight out of thirty-eight at some time showed symptoms of intolerance. Of thirty-two cases in which results could be assessed, eighteen appeared to be cured, in nine well-marked improvement took place and in five only moderate improvement. The treatment is useless in lupus erythematosus.

RINGWORM

The work of Duncan (1945) has shown that ringworm of the head in children is caused in the Midlands and North of England almost entirely by the "human" parasite *Microsporon audouini;* in London about equally by *M. audouini* and the "animal" (cat and dog) parasite *M. felineum.* In Devonshire, between Exeter and the coast, *M. felineum* predominates and is also widely distributed in other parts of Devon, Dorset and parts of Hampshire. In Portsmouth, *M. lanosum* (now regarded as the same species as *M. felineum*) is responsible for all the indigenous infections.

The importance of this is that infections of the scalp by *M. felineum* and *lanosum* can often be cured by local antiseptics, whereas *M. audouini* infections practically always require X-ray epilation.

Favus appears to be more widespread than it was. Duncan isolated *Achorion schœnleinii* from thirteen cases, eight of which were clinically

million units of penicillin intramuscularly; others are even more resistant.

Anthrax.—Penicillin is the treatment of choice, 15,000 units three-hourly for five days seems to be adequate.

Ill-effects of penicillin.—A dermatitis is set up not uncommonly by the base of the cream and less often by the solution, i.e., by the penicillin itself or an impurity. Intramuscular injections occasionally give rise to urticaria, erythema, œdema, fever and abdominal colic. .

SULPHONAMIDES

In cases of systemic streptococcal infection sulphonamides are usually sufficiently active and so much more convenient than penicillin that they are generally used first. Staphylococcal infections being less susceptible to sulphonamides should have penicillin from the start. Of the sulphonamides, my own preference is usually for sulphadimethyl pyrimidine (sulphamezathine) because it seldom upsets the patient; it is rapidly absorbed and relatively slowly excreted, so that a good concentration is maintained in the blood, and its excretion products being soluble there is little risk of blockage of the ureters. For dermatitis herpetiformis, however, sulphapyridine is the only sulphonamide which is of much use. When it is necessary to use a sulphonamide locally, sulphadiazine is the safest, applied in a strength of 5 per cent. in zinc cream or paste. Even this should not be used as a routine but only in cases which have resisted other local antiseptics. The risk of sensitizing the skin by the use of sulphanilamide or sulphathiazole powder is a very real one.

Peterkin (1945) has published an analysis of 500 cases of *sulphonamide dermatitis* in troops in North Africa and the Middle East, and records of 1,052 cases have been published by other authors. The most common eruption (61.8 per cent.) was due to light sensitization and took the form of œdema, bullæ and crusts. Another common type (10.2 per cent.) was contact dermatitis not due to light. This was vesicular and was followed by weeping, superficial ulceration and sometimes by general eczematization. The remaining cases were made up of about seventeen other types of eruption. In treatment, wet dressings of lead and calamine lotion, weak eusol or eau d'Alibour were best. For sepsis, penicillin cream, silver nitrate 2 per cent., or crystal violet 1 per cent. were used. Acriflavine, it should be remembered, must not be used in sulphonamide dermatitis, for it greatly aggravates it.

The question of *desensitization* of patients who are sensitive to sulphonamides is still debated. Tate and Klorfajn (1944) consider that desensitization can usually be achieved by giving very small doses, such as 0.125 gm. ($\frac{1}{4}$ tablet), twice daily. When a given dose ceases to cause a reaction it is doubled and so continued until it ceases to cause a reaction, then doubled again and so on until the patient can tolerate full doses.

ARSENICAL DERMATITIS

A compound called B.A.L. (British Anti-Lewisite) was developed in secret during the recent war and proved to be a valuable weapon in the treatment of arsenical dermatitis. It is not yet on the market but the dosage is said to be up to 4 mgm. per kgm. of body weight, given intramuscularly in oily solution at intervals of four hours. It should not be used in cases in which the liver is damaged (*Lancet*, 1945).

CALCIFEROL IN LUPUS VULGARIS

A great step forward in the treatment of lupus vulgaris has been taken by Dowling and Prosser Thomas (1946) in this country and by Charpy (1943) in France. These observers found independently that the administration of calciferol (vitamin D_2), to the extent of 150,000 international units daily by mouth, has a highly beneficial effect on the majority of cases of lupus vulgaris. Dowling and Prosser Thomas gave the calciferol in the form of high potency ostelin tablets (Glaxo) 50,000 units in each, one tablet being swallowed thrice daily. Charpy gave it in solution.

One hundred and fifty thousand units daily is as much as most patients can take without feeling sick and the dose has been reduced after varying periods to 100,000 or 50,000 units daily. Hypercalcæmia occurred in only three cases out of thirty-eight, levels of 12.6, 12.8, and 14.8 mgm. per 100 c.cm. of blood being recorded. These patients did not show any clinical symptoms of intolerance. Evidently clinical symptoms of poisoning are a better guide to the dosage being too high than is the blood calcium level; nausea, loss of appetite, depression or feeling out of sorts are the usual symptoms complained of. Of Dowling's patients, eight out of thirty-eight at some time showed symptoms of intolerance. Of thirty-two cases in which results could be assessed, eighteen appeared to be cured, in nine well-marked improvement took place and in five only moderate improvement. The treatment is useless in lupus erythematosus.

RINGWORM

The work of Duncan (1945) has shown that ringworm of the head in children is caused in the Midlands and North of England almost entirely by the "human" parasite *Microsporon audouini;* in London about equally by *M. audouini* and the "animal" (cat and dog) parasite *M. felineum.* In Devonshire, between Exeter and the coast, *M. felineum* predominates and is also widely distributed in other parts of Devon, Dorset and parts of Hampshire. In Portsmouth, *M. lanosum* (now regarded as the same species as *M. felineum*) is responsible for all the indigenous infections.

The importance of this is that infections of the scalp by *M. felineum* and *lanosum* can often be cured by local antiseptics, whereas *M. audouini* infections practically always require X-ray epilation.

Favus appears to be more widespread than it was. Duncan isolated *Achorion schœnleinii* from thirteen cases, eight of which were clinically

atypical. Atypical cases of favus without scutula have been shown at the Dermatological Section of the Royal Society of Medicine. Whittle also has called attention to them. Suspicion of favus should be aroused in any case of chronic patchy cicatricial alopecia with crusting and scaling, particularly if the scalp has a "mousy" odour.

Ringworm of the feet.—Phillips (1944) has published good results and no ill-effects in 230 army cases treated with the much publicized phenol-camphor. On the other hand, numerous warnings and unsatisfactory results have been published by other users. It is essential that no water should be added to the phenol-camphor mixture and that the skin should be dry when it is applied.

ANIMAL PARASITES

Scabies.—Mellanby (1945) found that "tetmosol" soap (containing 10 per cent. of tetraethyl thiuram monosulphide) was very useful in the prophylaxis of scabies in an asylum where scabies was endemic. The use of this soap in place of ordinary soap prevented new cases from arising and cured many patients who were already infected.

Pediculosis capitis.—Scobbie (1945) found that one application of five teaspoonsful of 2 per cent. D.D.T. emulsion to children's heads killed all lice and remained long enough on the head to kill all larvæ as they hatched out. A compress of 2 per cent. lysol applied to the head for eight hours after thorough wetting of the hair with the same solution was the most efficient application for killing nits *in situ*.

Pediculosis corporis.—The impregnation of soldiers' underclothing with 1 to 2 per cent. of D.D.T. in the recent war kept the wearers free from body lice, although not from crab lice, for about one month, in spite of weekly laundering. The blowing of inert powder containing 10 per cent. of D.D.T. under the clothes at five sites was very successful in controlling lice in civilian populations.

Pediculosis pubis.—The application of a 4 per cent. solution of D.D.T. in liquid paraffin or the rubbing in of 10 per cent. of D.D.T. in an inert powder is said to be an effective cure for pediculosis pubis.

Bed bugs.—Spraying of the walls and furniture with a 5 per cent. solution of D.D.T. in kerosene, in such amount that at least 100 mgm. of D.D.T. per square foot is deposited, renders the treated surfaces lethal to bugs for three months.

Dangers of D.D.T.—In the usual concentrations (5 and 10 per cent.) and amounts used as insecticides and parasiticides, especially in powder form, D.D.T. is harmless to man, although some cats and dogs have died from its application. Care must be taken that it is not swallowed and that prolonged exposure does not take place to oily solutions which might be absorbed. The symptoms of poisoning are tiredness and irritability, heaviness and aching of the limbs, muscular weakness, fine tremors and, finally, respiratory failure. Chronic poisoning by small doses leads to anorexia and damage to the liver and kidneys.

INSECT REPELLENTS

Dimethyl phthalate, a colourless oily liquid, was largely used in South-East Asia to repel mosquitoes. Sprayed on the clothing it was effective for about a week and for a few hours if rubbed over the skin. It is applied to the skin by pouring a little on the hands, rubbing these together and then smearing them over the parts of the skin to be protected. The eyelids, lips and scrotum should be avoided, as in these places it causes irritation. It should be kept off artificial silk and nylon, also off spectacle frames, fountain pens, buttons and the like made of certain plastics, as these are dissolved by it. For the familiar midge an emulsion containing 50 per cent. of dimethyl phthalate seems to be strong enough (*Brit. med. J.*, 1946). Dibutyl phthalate was much used in South-East Asia for protecting troops from the bites of the mites carrying scrub typhus which are related to our familiar "harvesters". Clothing smeared or impregnated with this compound killed the mites before they could reach the skin. Dimethyl phthalate acted twice as quickly, but was more readily washed out of the clothing (Lewthwaite, 1945).

CONDYLOMATA ACUMINATA

A very useful treatment for these troublesome warts was introduced by Culp, Magid and Kaplan (1944). A 25 per cent. suspension of podophyllum resin in liquid paraffin is applied thoroughly to the whole warty area for eight hours at a time. It is then washed off and a dusting powder applied. The warts shrivel up and turn yellow in twenty-four hours and fall off in two or three days. If all the warts are not cured at the first attempt repeated applications may be made, but none should remain on for longer than eight hours at a time or dermatitis may result. In my experience this treatment is useless for any other type of wart.

ŒSTROGENS

Barber (1946) has called attention to the skin disorders of the menopause and their treatment by œstradiol or synthetic œstrogens. Synthetic œstrogens are also useful, as the same observer has pointed out, in adolescent acne vulgaris in both sexes, helping to restore the balance between œstrogens and androgens, which latter are said to preponderate in cases of acne.

References

Barber, H. W. (1946): *The Practitioner*, 156, 333.
Brit. med. J. (1946): i, 583.
Charpy, M. J. (1943): *Ann. Derm. Syph.*, 11 and 12, 331.
Culp, O. S., Magid, M.A., and Kaplan, I. W. (1944): *J. Urol.*, 51, 655.
Dowling, G. B., and Prosser Thomas, E. W. (1946): *Brit. J. Derm. Syph.*, 58, 45.
Duncan, J. T. (1945): *Brit. med. J.*, ii, 715.
Lancet (1945): ii, 854.
Lewthwaite, R. (1945): *Brit. med. Bull.*, 3, 227.
Mellanby, K. (1945): *Brit. med. J.*, i, 38.
Peterkin, G. A. G. (1945): *Ibid.*, ii, 1.
Phillips, B. (1944): *Brit. J. Derm. Syph.*, 56, 219.
Scobbie, E. B. S. (1945): *Brit. med. J.*, i, 409.
Tate, B. C., and Klorfajn, I. (1944): *Lancet*, ii, 553.

ADVANCES IN THE TREATMENT
OF VIRUS DISEASES

WITH PARTICULAR REFERENCE TO INFLUENZA AND THE COMMON COLD

By C. H. STUART-HARRIS, M.D., F.R.C.P.

Professor of Medicine, University of Sheffield.

THE central problem in the development of specific methods of attack on virus infections is the location of the virus within the cells constituting the lesions. For the virus is an organism which only undergoes multiplication within the protecting wall of the cell membranes of the host. Its intracellular location enables it to obtain the raw materials needed for its multiplication directly from the host cells, which are thereby modified and often destroyed. Release of the virus by death of the infected cell brings about an extracellular phase which is speedily followed by further penetration of other cells and spreading of the lesion. Some viruses appear to spend their days wholly within a particular type of epithelium or tissue to which they gain access and thus produce an essentially localized infection, but others circulate in the blood stream and multiply within the cells of many different tissues. Now, bacteria are essentially extracellular in location within the host and can be reached readily by chemicals circulating in the blood or lymph. Thus either their multiplication may be arrested, as for instance by sulphonamide compounds, or they may be killed by antiseptics, or both types of action may occur, as with penicillin. The fact that the phase of virus multiplication is protected by the barrier of the cell membrane means that, if successful chemotherapeutic action is to occur, antiviral agents must theoretically possess specific powers of penetration through cell membranes and of attack on the virus without thereby destroying the host cell. However, there is no theoretical reason, according to the chemists, why chemical agents with these properties should not ultimately be found, and in any case, if the virus can be attacked during the phase of circulation in the blood or of spread from one cell to the next, the size of the lesion may be limited. It may be that the few known instances of specific virus chemotherapeusis are effected in one of these two ways. The scope of different chemotherapeutic agents in the treatment of virus diseases will now be briefly described, and the particular problems of virus infections of the respiratory tract will then be discussed.

THE SULPHONAMIDE COMPOUNDS

In spite of intensive search, few instances of successful therapy of virus diseases with sulphonamide compounds have been discovered in which the actual lesions due to the virus are favourably influenced. However, both lymphogranuloma inguinale and trachoma are thus benefited and in the case of the former disease treatment with sulphapyridine or sulphathiazole

is now established, although antimonial compounds are often used as well. There have been interesting developments in the treatment of rickettsial infections, and particularly of typhus fever, with agents related to the sulphonamides. The first of these was the discovery by Andrewes and his co-workers (1944) that certain benzamidine drugs possessing a sulphonamide radicle (V.147 and V.186) exerted a favourable influence on the experimental infection of mice by rickettsia of epidemic or murine typhus. Unfortunately this favourable effect was not demonstrated in the case of human typhus, possibly because of the difficulty of initiating therapy at a sufficiently early stage of the disease and of an undue toxicity of the drugs for the human body. A more successful development was that sponsored by Snyder and his co-workers (Yeomans *et al.*, 1944), who first demonstrated that para-amino-benzoic acid (PABA), which usually causes a reversal of the bacterio-static activity of sulphonamides, was actively inhibitory to experimental rickettsial infection. They further claimed that in human typhus large doses of PABA would ameliorate the disease and lower mortality. Favourable action of PABA against experimental tropical typhus of the Far Eastern countries has also been demonstrated (Snyder and Zarafonetis, 1945). The importance of all these developments appears to lie in the fact that they have shown that virus diseases can be favourably influenced by chemical agents, and as such they may point the way to further advance.

There is at present wider scope for the sulphonamides in the treatment of the bacterial complications of virus diseases. Although the reason for the peculiar tendency of virus infection to open the door for secondary bacterial attack is far from clear, there is no doubt that the severity of the resulting virus-cum-bacterial disease is often due to the action of the bacterial component. Thus sulphonamides are useful in the treatment of severe confluent smallpox although they possess no demonstrable action on variola virus. Perhaps they effect a limitation of secondary staphylococcal multi-plication within the pustule. When smallpox is complicated by hæmolytic streptococcal infection, as in the outbreak described by Wilkinson (1942), even better effect may be obtained with sulphonamides. Another instance of successful sulphonamide therapy is that recorded by Banks (1942) in the case of measles, in which prophylactic therapy instituted at an early stage of illness may prevent suppurative complications in the ears or pneumonic complications of the chest. The treatment of bacterial complication in the case of other virus diseases of the respiratory tract will in general be better instituted when such complication has developed, although some authors (Finland *et al.*, 1942) recommend routine use of sulphonamides in the case of influenza as a prophylactic against complications.

PENICILLIN

Three virus agents are demonstrably affected by penicillin—epidemic typhus rickettsia, psittacosis, and the virus of inclusion conjunctivitis.

With the first two viruses, however, enormous doses of penicillin are needed to influence the experimental disease and Bedson and May (1945) estimate that 11 mega units would be required to treat a human case of psittacosis. Although one or two isolated cases of human psittacosis have been successfully treated with penicillin, it is doubtful if penicillin constitutes a really effective remedy. Certainly in the case of typhus, average doses of penicillin fail to influence the human disease in any way. Inclusion conjunctivitis appears to be in an entirely different category and Sorsby (1945) claims that in the infant, local therapy with a weak solution of penicillin (2,500 units per c.cm.) produces dramatic benefit.

In bacterial complications of virus diseases, on the other hand, penicillin therapy is more likely to be generally successful. Thus, in confluent smallpox penicillin may have a dramatic effect and cause a simple desiccation of the pustule with relief of toxæmia, instead of the usual sloughing and widespread purulent exudation. On the other hand, penicillin therapy in practice necessitates parenteral use and no case has been made out for the indiscriminate treatment of a virus disease, such as measles, in the hope of preventing suppurative complications. More will be said later about the use of penicillin in the treatment of established bacterial complications.

GAMMA GLOBULIN

Fractionation of the proteins of human plasma by the use of the methods elaborated by Cohn and co-workers in the United States (1944) was carried to an advanced stage during the recent war. The fraction known as gamma globulin contains most of the serum antibodies, including antiviral substances effective against influenza, measles and mumps. Its antibody content is some 10 to 30 times that of normal serum, and preparations from recently convalescent individuals would presumably be even more potent. Owing, however, to the general inability of antibody to influence virus infection of the cell once invasion has occurred there is little theoretical justification for a belief that gamma globulin would be of much value as a therapeutic weapon, although it is a valuable prophylactic in the prevention or attenuation of measles. Claims to attenuate or abort the disease when given in the pre-eruptive stage (Stokes, Maris and Gellis, 1944) should therefore be received with caution. The history of serum therapy for poliomyelitis is too recent to permit enthusiasm for a similar claim in the case of measles. It has also been claimed that the complications of mumps are lessened by gamma globulin given during the disease, but here again caution is advised. It is, however, certain that more will be heard of this new product, and it is to be hoped that it will soon be freely available for trial in this country.

THE COMMON COLD

The acclaim which greets each new reputed "cold cure" is an indication of the present impotence to prevent or to limit that commonest of all virus infections. Since the failure of patulin to abort the common cold, no gleam

of hope has appeared to lighten the gloom of the man-in-the-street or the physician afflicted by the disease, unless it be the news that a concerted laboratory offensive upon the etiological agent is to be opened on both sides of the Atlantic. Much was hoped from attempts to limit secondary bacterial invasion by means of sulphonamides or penicillin administered locally or generally. Although there is no reason to doubt that measures such as sulphadiazine by mouth (Cecil, 1945) or penicillin used as a snuff (Delafield, Straker and Topley, 1941) cause a considerable reduction in the naso-pharyngeal bacterial flora, such improvement is not consistently accompanied by a remission of symptoms. Cecil writes that it is necessary to be prepared for the view that the common cold virus not only attacks the nasopharyngeal mucosa but also the adjacent tubes and cavities as well. Fundamental work still has to be done before the relative importance of virus and bacteria in the etiology of the common cold will be understood. Certainly chemotherapy should be restricted to the treatment of those acute complications, such as otitis media or sinusitis, demonstrably due to a hæmolytic streptococcus, a pneumococcus or a pyogenic staphylococcus. A consensus of opinion on the value of chemotherapy in the treatment of such acute complications would be undoubted, and either sulphonamides by mouth or penicillin by injection can be utilized. Local use of sulphonamides, such as microcystalline sulphathiazole or sulphadiazine (2.5 per cent. sulphadiazine in 8 per cent. triethanolamine solution), by spray is advocated by some for acute complications; others recommend penicillin solution containing 200 to 500 units per c.cm., but the difficulty of obtaining entrance to closed cavities must not be forgotten, and, in view of the undoubted effect of general administration, local use is of debatable value.

ATYPICAL PNEUMONIA

Atypical pneumonia of virus origin has in part achieved recognition because of the impotence of present chemotherapeutic agents to influence its course. Thus an infection with predominant involvement of the respiratory tract which shows complete lack of response to sulphonamides or to penicillin should always be investigated further with an eye to the possibility that the condition is one of primary atypical pneumonia. If the leucocyte count is not elevated and if the X-ray of the chest reveals the characteristic veiled opacity of atypical pneumonia, then further chemotherapy is useless. The general failure of all but symptomatic therapy in primary atypical pneumonia would indeed be alarming if it were not for the fact that the disease is hardly ever fatal.

INFLUENZA

Although much knowledge concerning the influenza viruses and the part played by these agents in the causation of human epidemics has been assembled in recent years and prophylaxis by means of specific virus vaccines is no longer a remote possibility, less progress has been made in

With the first two viruses, however, enormous doses of penicillin are needed to influence the experimental disease and Bedson and May (1945) estimate that 11 mega units would be required to treat a human case of psittacosis. Although one or two isolated cases of human psittacosis have been successfully treated with penicillin, it is doubtful if penicillin constitutes a really effective remedy. Certainly in the case of typhus, average doses of penicillin fail to influence the human disease in any way. Inclusion conjunctivitis appears to be in an entirely different category and Sorsby (1945) claims that in the infant, local therapy with a weak solution of penicillin (2,500 units per c.cm.) produces dramatic benefit.

In bacterial complications of virus diseases, on the other hand, penicillin therapy is more likely to be generally successful. Thus, in confluent smallpox penicillin may have a dramatic effect and cause a simple desiccation of the pustule with relief of toxæmia, instead of the usual sloughing and widespread purulent exudation. On the other hand, penicillin therapy in practice necessitates parenteral use and no case has been made out for the indiscriminate treatment of a virus disease, such as measles, in the hope of preventing suppurative complications. More will be said later about the use of penicillin in the treatment of established bacterial complications.

GAMMA GLOBULIN

Fractionation of the proteins of human plasma by the use of the methods elaborated by Cohn and co-workers in the United States (1944) was carried to an advanced stage during the recent war. The fraction known as gamma globulin contains most of the serum antibodies, including antiviral substances effective against influenza, measles and mumps. Its antibody content is some 10 to 30 times that of normal serum, and preparations from recently convalescent individuals would presumably be even more potent. Owing, however, to the general inability of antibody to influence virus infection of the cell once invasion has occurred there is little theoretical justification for a belief that gamma globulin would be of much value as a therapeutic weapon, although it is a valuable prophylactic in the prevention or attenuation of measles. Claims to attenuate or abort the disease when given in the pre-eruptive stage (Stokes, Maris and Gellis, 1944) should therefore be received with caution. The history of serum therapy for poliomyelitis is too recent to permit enthusiasm for a similar claim in the case of measles. It has also been claimed that the complications of mumps are lessened by gamma globulin given during the disease, but here again caution is advised. It is, however, certain that more will be heard of this new product, and it is to be hoped that it will soon be freely available for trial in this country.

THE COMMON COLD

The acclaim which greets each new reputed "cold cure" is an indication of the present impotence to prevent or to limit that commonest of all virus infections. Since the failure of patulin to abort the common cold, no gleam

by steam inhalations medicated with eucalyptus or Friar's balsam and a simple expectorant. The duration of rest in bed needs to be adjusted to the severity of the disease and the age of the patient. Young adults are usually fit enough to be up within a day of the termination of the fever but caution must be exercised in patients with signs of bronchial involvement or in the elderly, in whom convalescence is much slower.

Influenzal pneumonia, as stated above, may synchronize with the influenza but more usually it follows it within a brief period. The onset of pulmonary involvement is then often heralded by the sudden development of pain in the chest of pleuritic type or by an unusual degree of cyanosis or dyspnœa. The most dangerous type of pneumonia, which is fortunately rare in current experience, is that due to the combined action of influenza virus and a *Staphylococcus aureus*. The total duration of this disease, which may attack young adults, may be only a matter of hours, and after an acute onset with severe headache, shivering and prostration, the subject becomes cyanotic and extremely dyspnœic with a rapid pulse. Pain in the chest may be absent and signs of pulmonary involvement may be minimal and confined to limitation of movement of the bases, indicative of engorgement which is speedily followed by œdema and exudation into the bronchioles. There is no time to lose in the treatment of such a case, and penicillin by intra-muscular injection and sulphathiazole or sulphadiazine by mouth should be given in maximal doses. Thus a dose of 100,000 or 50,000 units of penicillin should be given at once and followed by 40,000 units every three hours. Sulphathiazole in a dose of 4 gm. initially should be continued with 2 gm. in four hours' time and then 1 gm. at four-hourly intervals. The patient should be nursed sitting-up and oxygen should be given. Such treatment has given encouraging results in recent experience, and the chief menace to the patient from this distressing form of the disease is that it should be unrecognized until the pulmonary involvement has progressed too far.

Such cases, however, constitute only a fraction of the total cases of pulmonary involvement in influenza epidemics. Commonest of all is an ill-defined condition which appears to be a *bronchiolitis* rather than a true consolidation of the lung. The signs in the chest consist of areas of weak breathing with crepitations and fine râles which may suggest small areas of consolidation, not demonstrable, however, by X-ray. The sputum in such cases consists of pellets of viscid muco-purulent material which yields a mixed flora on culture. This condition does not seem to respond to chemo-therapy with any regularity, thus supporting the view that it is due essentially to a virus lesion of the bronchiolar epithelium rather than to bacteria. Although signs in the chest and sputum may continue for several days the ultimate outlook is good and recovery is usually complete. The occurrence of bronchiolitis or simple bronchitis in an attack of influenza in a subject with emphysema is not, however, such a simple affair. Particularly in elderly subjects, the attack may precipitate right-sided heart failure with venous congestion and severe cyanosis. Oxygen therapy is then the only

relation to the treatment of the disease. No known chemotherapeutic agent is active against infection by the virus once this has been acquired. The very fact that penicillin and sulphadiazine are now used to aid isolation in the chick embryo of the virus from human garglings adds colour to this bald statement. On the other hand, immune serum has been shown to be effective in limiting the spread of the virus attack in the case of the experimental influenza virus pneumonia of mice. Serum is, however, impotent to limit the experimental disease of the ferret unless the latter is accompanied by lung involvement due to the virus. In the latter circumstances an intranasal spray of serum may limit the extent of lung involvement, yet the fever and nasal symptoms are entirely unaffected. In man, parenteral serum is without effect once the disease has begun, and attempts to control spread of infection by inhalation of atomized serum have been in general unsuccessful.

Recent epidemics of influenza have shown a mortality chiefly in the aged and the very young, and in these it is the tendency of the virus attack to initiate a bacterial infection of the lungs, of the nasal sinuses or of the middle ear, which is responsible for the severe complications. The exact relationship between the virus and the bacteria is obscure, particularly in that the pneumonia following influenza may develop within a few hours, days or even weeks after the onset of the attack. Also, post-influenzal pneumonia is as likely to follow a trivial as a severe attack of influenza. Under epidemic conditions it is fortunate that serious pulmonary complications are usually uncommon, although pandemics such as those of 1890 and 1918 must be excepted. The general mildness of recent epidemics has been attributed by some to the routine administration of sulphonamide drugs, for there is little doubt of the frequency of this practice. No controlled trial, however, has been made of the attempted prophylaxis of complications of influenza by the routine administration of sulphonamides, and the fact that the incidence of such complications is normally low would argue against such routine use without proof of its value. The truth is more likely to be that the character of the influenza viruses prevailing in recent years has not favoured a general attack upon the lung. No-one can foresee whether or not a more virulent strain with particular power to attack the lung and to initiate bacterial complications may appear in the future, but this possibility cannot be excluded. If such a strain did appear, routine prophylaxis by chemotherapeutic agents and a possible trial of immune serum by intranasal administration would undoubtedly be justified.

TREATMENT.—The treatment of the ordinary case of mild influenza consists of confinement to bed until the end of the fever. Symptomatic treatment for the headache, general aching and cough may be needed, and aspirin, Dover's powder, or aspirin combined with codeine [$\frac{1}{4}$ grain (0.015 gm.)] are useful drugs. If a useless, irritating cough causes distress, a linctus such as the familiar Gee's linctus or repeated doses of codeine may be needed. A severe degree of laryngitis or tracheitis is usually helped

ADVANCES IN UROLOGY

By R. H. O. B. ROBINSON, F.R.C.S.

Surgeon, St. Thomas's Hospital; Consulting Urological Surgeon to the Ministry of Pensions.

THE advances which have been made recently in the field of urology are for the most part modifications of, or additions to, tried technique. Some advances are revolutionary, such as the application of penicillin in this branch of surgery, the use of synthetic œstrogens in the treatment of carcinoma of the prostate, and the retropubic approach in prostatectomy.

INFECTIONS OF THE URINARY TRACT

The treatment of infection in the urinary tract has been profoundly modified by the introduction of the sulphonamides and penicillin.

The sulphonamides exert a notable effect on *B. coli,* gonococci, streptococci and, to a more variable extent, on staphylococci. They have little appreciable effect on *B. proteus* and none on *B. tuberculosis.* For the treatment of acute infections due to *B. coli,* forced fluids and alkaline therapy are indicated with the use of sulphonamides in moderate doses. Small doses are liable to produce sulphonamide-resistant strains of organisms, and there is nothing to be gained by excessive dosage, as this may lead to the precipitation of sulphonamide crystals in the renal tubules and renal pelvis, thereby producing hæmaturia, renal colic and even suppression of urine. Certain sulphonamides are more prone to precipitate, particularly sulphapyridine, and especially if the urine is allowed to become acid or concentrated. Such a crisis is dealt with by alkalis and forced fluids with, if necessary, cystoscopy and the passage of ureteric catheters through which the crystals can be washed out of the renal pelves. A new method of relief worthy of trial is novocaine injection of the sympathetic trunk, which relieves spasm and colic and which, with fluids, may lead to the passage of the obstructing crystals. Sulphathiazole or sulphadiazine should be given with an initial dose of 2 gm. followed by 1 gm. four-hourly, up to a total dose of 20 gm. In cases of *B. coli* infection in which relapse is encountered, treatment is best carried out with one of the preparations of mandelic acid. To achieve the best results this demands a low fluid intake, with consequent restricted output and a highly acid urine. Relapse, however, suggests that there is some abnormality present in the urinary tract, and necessitates a complete urological investigation.

Penicillin inhibits staphylococci, streptococci and anaerobes, but has no influence on *B. coli, B. proteus* or *B. tuberculosis.* It has particular value in staphylococcal infections of the cortical part of the kidney, often manifested in the clinical condition of renal carbuncle. The presence of staphylococci may be difficult to establish in the urine and it is essential to examine stained deposits spun down in a high-speed centrifuge. The diagnosis may

remedy available to tide the patient over the crisis. Both in influenzal bronchiolitis and bronchitis, the use of penicillin by inhalation has yet to be fully explored. The significance of penicillin-resistant gram-negative organisms (*Hæmophilus influenzæ*) in the etiology of these conditions is not, however, fully understood and inhalation may, by elimination of susceptible bacteria, permit an increase of the resistant organisms, which are in fact just as pathogenic as the others.

In between the extremes of fulminating pneumonia and bronchiolitis are the majority of cases recognizable as instances of actual consolidation. In recent epidemics these have been due chiefly to the pneumococcus and appear to respond as well to chemotherapy as does pneumonia unassociated with influenza. According to the severity of the condition and availability of the agents, penicillin or sulphapyridine, sulphathiazole, sulphadiazine or sulphamezathine may be utilized. Thus the treatment of such complications or, for that matter, of other bacterial complications, such as sinusitis or otitis media, does not differ from that which would be employed if influenza virus had not been the responsible precipitating agent of the condition.

CONCLUSION

In conclusion, it may be justly commented that the treatment of the vast field of virus disease is almost virgin soil for the experimental chemotherapist. The accomplishments in the field thus far, although encouraging, have achieved little practical significance except for the combat of secondary bacterial invasion. It is not possible to conclude, however, without reference to the striking advances achieved in the prevention of virus diseases. No better instances could be given of the advance in specific preventive measures than the success of yellow fever vaccine or, for that matter, of sero-prophylaxis of measles. In the case of influenza, trials of the concentrated refined vaccine of Francis and co-workers (1944) are still required before its scope can be fully established, but there is little doubt that the vaccine represents a substantial advance on earlier products.

References

Andrewes, C. H., van den Ende, M., King, H., and Walker, J.(1944): *Lancet*, i, 777.

Banks, H. S. (1942): *The Practitioner*, **149**, 297.

Bedson, S. P., and May, H. B. (1945): *Lancet*, ii, 394.

Cecil, R. L. (1945): *Bull. N.Y. Acad. Med.*, **21**, 263.

Cohn, E. J., *et. al.* (1944): *J. clin. Invest.*, **23**, 417.

Delafield, M. E., Straker, E., and Topley, W. W. C. (1941): *Brit. med. J.*, i, 145.

Finland, M., Peterson, O. L., and Strauss, E. (1942): *Arch. int. Med.*, **70**, 183.

Francis, T., Salk, J. E., Pearson, H. E., and Brown, P. N. (1944): *Proc. Soc. exp Biol. N.Y.*, **55**, 104.

Snyder, J. C., and Zarafonetis, C. J. D. (1945): *Ibid.*, **60**, 115.

Sorsby, A. (1945): *Brit. med. J.*, i, 903.

Stokes, J., Maris, E. P., and Gellis, S. S. (1944): *J. clin. Invest.*, **23**, 531.

Wilkinson, P. B. (1942): *Lancet*, ii, 67.

Yeomans, A., *et al.* (1944): *J. Amer. med. Ass.*, **126**, 349.

under œstrogenic treatment. As a rule, the development of the tumour and its metastases is associated with an elevation of the acid serum phosphatase and this is particularly marked when metastasis has taken place. The reduction of this to normal levels is the most accurate criterion for assessing the dosage of synthetic œstrogens. Not all cases, however, show this rise and fall and the clinical features of overdosage with œstrogens can then be used as a guide: these are breast changes, pigmentation, diminished sexual activity with atrophy of the testes, dizziness and vasomotor disturbances. An average dose of 15 mgm. of stilbœstrol per diem is given until obvious clinical response or undesirable side-effects indicate its reduction to a maintenance level of 1 to 2 mgm. per diem. American urologists consider that castration controls the growth of both primary tumours and metastases to a greater degree than synthetic œstrogen therapy alone. Neither form of treatment appears to afford any protection against the development of secondaries. An argument against the operation of orchidectomy alone is the evidence that the body can elaborate androgenic substances outside the testis and that after orchidectomy this extragenital androgen output may be increased, demanding synthetic œstrogens to counteract it.

The value of combining œstrogenic therapy and radiotherapy in the treatment of both the primary tumour and its metastases is still doubtful. If retention should develop, and it is usually avoided by energetic treatment, transurethral resection of obstructing prostatic tissue will become necessary. After resection, an indwelling catheter in the urethra will be necessary for two or three days, and for this purpose the Foley catheter is superior to any other. This is an American rubber catheter with multiple eyes and an inflatable rubber bag near the tip which can be blown up once the catheter has been introduced into the bladder, thereby preventing its removal until the bag has been emptied. It can also be used for hæmostasis by pulling on the external end and drawing down the distended bag into the bladder neck. No external or constrictive fixation to the penis is required and therefore sepsis is reduced to a minimum.

BENIGN ENLARGEMENT OF THE PROSTATE

In the treatment of benign enlargement of the prostate the most notable advance has been the introduction of *retropubic prostatectomy* by Millin. It will be remembered that the alternative and older routes of approach to the gland are the suprapubic, the perineal and the transurethral. This last is often referred to as the perurethral. The possibility of approach through the cave of Retzius and false capsule had previously been considered too hazardous, principally because of the fear of sepsis. The introduction of the sulphonamides and penicillin has largely removed this bogey. The operation would appear to be ideal for markedly enlarged prostates, particularly of the type in which hyperplasia of the lateral lobes exists. Although it can be carried out as the second stage of a two-stage procedure, technically the operation is considerably more difficult when the surgeon

largely turn on radiological findings: namely, lack of respiratory mobility of the kidney, blurring of the edge of the psoas muscle shadow and changes in the pyelogram resembling those seen in neoplasm. Perinephric abscess may occur as a complicating factor and may require incision and drainage: penicillin is instilled locally into the cavity. Penicillin may also be found of great use as an adjunct to surgery in such conditions as traumatic lesions, post-operative infections and extravasation of urine with secondary infection. Administration is carried out in the usual manner by repeated intramuscular injections of 30,000 units, at three-hourly intervals for from three to six days; but in the case of a localized infected cavity the drug should be introduced directly, and it is most useful in the invasive stage before localization has had time to take place. It has been found that staphylococcal infections require roughly twice the dosage necessary in streptococcal infections.

URINARY CALCULI

From time immemorial it has been hoped that some substance would be discovered having a solvent action on urinary calculi, thus protecting the tissues from their harmful secondary effects and abolishing the necessity for surgery. The discovery by Suby and his collaborators of "solution G" has raised high hopes. It aims at transforming insoluble calcium phosphate into soluble calcium citrate. In the case of pure phosphatic stones or incrustations in a simple cavity such as the bladder, good results have been obtained. On the other hand, in the case of mixed stones, or in such a complicated and relatively inaccessible cavity as the renal pelvis, the results are disappointing. It has been known for some time that in patients with calculi the output of citric acid in the urine is well below normal levels even when the blood level is unaffected, and it would appear that there is in these patients some mechanism for breaking down citric acid to an excessive degree. It is therefore unlikely that oral administration of citric acid will have any significant effect on existing calculi, however large the dose. Irrigation of the mucosa of the bladder or renal pelvis with a solution of sodium citrate and citric acid leads to necrosis of the epithelium. Suby discovered that the addition of magnesium oxide eliminated this effect without impairing the solvent properties. The most impressive results are obtained in alkaline incrustation of the bladder, which is cured by continuous drip irrigation of solution G for one to three weeks. Solution G also has definite bactericidal power, due probably to its high acidity (pH 4.0).

CARCINOMA OF THE PROSTATE

The treatment of carcinoma of the prostate has been profoundly influenced by the discovery of the benefits of œstrogenic substances. In the majority of cases the disease originates in the posterior lobe of the gland and this renders it possible to obtain material for biopsy if a transurethral resection is carried out as part of the treatment. Such material examined after successive resections will show a marked regression of the malignant cells

From the point of view of nursing and personal comfort of the patient this is a tremendous advance on any other operation, with the exception of the transurethral. It also avoids any risk of trauma to the urethra and resultant stricture which is one of the bugbears of the transurethral approach.

These considerations lead inevitably to an attempt to evaluate the *transurethral operation*. This, in the hands of an experienced and careful operator, is ideal for middle-lobe enlargement and fibrous bars at the bladder neck. It can be used with great success in cases of gross enlargement, always provided a really adequate resection is carried out, and has the advantage of being the most suitable operation in bad operative risks. This has been emphasized by Wardill and more recently by Stewart.

NEPHRECTOMY IN HYPERTENSION

The most interesting recent advance in renal surgery is the place of nephrectomy as a treatment of hypertension, following the pioneer experimental work of Goldblatt. His researches indicate that renal hypertension is the result of a humoral factor elaborated within an ischæmic kidney. Therefore this possibility must be considered in all patients with hypertensive symptoms, and a complete renal investigation must be carried out by differential renal function tests and pyelography, both intravenous and retrograde. Unfortunately, only a small number of patients in whom the operation of nephrectomy seems clearly indicated derive benefit, and it is essential that operation should be carried out before irrevocable vascular changes have occurred in the opposite kidney. The exact effect cannot be gauged from the immediate result, which is always to a certain degree beneficial. At least a year must elapse before a cure can be considered to have taken place. Cases of atrophic pyelonephritis are the most promising; but almost any solitary renal lesion may initiate the syndrome and nephrectomy lead to its disappearance.

PENILE WARTS

An interesting innovation in therapeutics is the use of podophyllin in the treatment of warts, which are very common around the external genitalia and anus. Podophyllin root is ground up and mixed as a twenty-five per cent. suspension in paraffin oil. This is applied to each individual wart, taking care that no excess of fluid is applied. One application is as a rule efficacious, and for penile warts the treatment appears superior to any other.

UNDESCENDED TESTICLE

The use of gonadotropic hormones in the treatment of imperfect descent of the testis now rests on clearer indications. For ectopic testis no benefit can be expected, as the testis has descended on an abnormal route and operation as soon as a definite diagnosis can be made is the correct treatment. In many cases the testicle or testicles descend normally at the time of puberty, and it is therefore inadvisable to induce precocious puberty by the use of hormones. If puberty is delayed, they may be tried; but if there is no result, operation must be considered.

has to deal with a pre-existing suprapubic bladder fistula. Further, with an open bladder some degree of sepsis is inevitably present, and it is considerably easier and safer to remove the prostate suprapubically through the bladder. In many cases these difficulties can be avoided by draining the bladder through an indwelling urethral catheter for a few days prior to retropubic prostatectomy. If the urine is infected a course of sulphonamide should be given. In cases in which the gland is not appreciably enlarged the operation is much more difficult to carry out and a better solution is to carry out transurethral prostatectomy. Again, in frank malignancy or inflammatory fibrosis of the bladder neck the operation is contraindicated. The main steps of retropubic prostatectomy are as follows:—

Having anæsthetized the patient by some method which ensures complete relaxation of the lower abdominal wall, the bladder is emptied completely by passing a rubber catheter. A moderate Trendelenburg position is then adopted and a median incision some four inches long made immediately above the symphysis pubis. A self-retaining retractor is then inserted separating the recti muscles and thereby exposing the front of the bladder below the peritoneal reflection. The bladder is now pressed upwards and backwards and held there by a pad of gauze fixed either by a third blade to the retractor or by the hand of an assistant. The anterior surface of the false capsule of the prostate now becomes visible in the lower part of the wound, covered by variable quantities of fat and dilated veins running largely from below upwards.   The most prominent of these are the tributaries of the dorsal vein of the penis. These are now tied by transfixion with stitches in two places above and below and divided between the two ligatures. The fat and ligatured veins are now pushed away by blunt dissection with gauze. At the upper part of the false capsule the transverse fibres of the internal sphincter of the bladder can be seen and possibly also arteries on the lateral portions of the capsule. These are tied by transfixion ligatures which are most easily introduced with a boomerang needle. At this stage two pads of gauze may with advantage be pushed back on each side of the prostate, holding any fatty tags out of the field of operation.   The false capsule is now opened transversely by a diathermy cutting current. This incision is across the anterior surface half-way between the apex below and the internal sphincter above.   Further dissection in the same plane and at some depth divides the true capsule of the prostate and renders visible the white adenomatous tissue. The anterior wall of the prostatic urethra is now open and the catheter can be felt lying in it. Enucleation of the gland is carried out in much the same manner as in suprapubic prostatectomy. The adenomatous mass is brought up into the wound, and is usually found to be adherent around the bladder neck. This attachment is preferably cut away with the diathermy current. Care must be exercised at this stage not to leave behind an isolated middle lobe or to leave irregular tags around the neck of the bladder. This, when viewed from below in the wound, gives an appearance not unlike that of the cervix uteri. The urethral catheter is drawn up through the prostatic space and fed through the open bladder neck into the bladder. The true and false capsules of the gland are now approximated in the transverse plane by interrupted stitches, preferably in two separate layers. Sulphonamide powder is insufflated into the cave of Retzius and a rubber drain inserted. The recti are approximated with interrupted catgut sutures and the skin edges sutured, the drain being brought out at the lower end of the incision. The urethral catheter is secured to the penis and syringed through to ensure that free drainage is taking place, and the patient is returned to bed.

The important point in the after-treatment is to make certain by adequate irrigation that the urethral catheter remains patent. The drain is removed in forty-eight hours and the catheter in four days. The patient is encouraged to get out of bed at the end of forty-eight hours. Some leakage of urine may occur from the lower part of the incision for a few days; but usually the wound remains dry and is soundly healed in ten days.

enter the eye itself. In man, subconjunctival injections of up to 500 units are well tolerated and give satisfactory and well-sustained levels in both aqueous and vitreous fluids. In desperate cases of intra-ocular infection, injections can be made into the anterior chamber or into the vitreous cavity. The amount that can be so injected seems to depend upon the purity of the specimen used; the drug does not readily diffuse out of the eye, and aqueous and vitreous concentrations remain high for several hours (Sorsby, 1945a, for references to experimental work).

Clinical.—Ulcerative blepharitis, acute and subacute conjunctivitis and infective corneal ulcers respond well to penicillin, and most of the bacteria found in such conditions seem to be sensitive. The time taken for cure varies, the more chronic diseases, such as blepharitis, may take some weeks. The frequency of application should vary directly with the severity of the infection but should not be less than three times daily. Chronic conjunctivitis, in which the infective element is less important and the symptoms are due more to vascular congestion, glandular hyperactivity, or allergy, responds poorly or not at all. Some few cases of acute conjunctivitis prove resistant and some relapse after initial cure (Brown, 1946; Fraser and Scott, 1946).

With intra-ocular inflammations, it is necessary to differentiate clearly whether they be due on the one hand to bacterial infections, or on the other to circulating toxins or allergens. The first group includes post-operative and wound infections and the metastatic endophthalmitis occurring in meningitis, measles or other exanthemas. These cases may respond well to penicillin if it be used sufficiently early; it is best given by subconjunctival or intra-ocular injection (Mann, 1946a).

Into the second group fall cases of acute and recurrent iritis, iridocyclitis, and choroiditis. In these no bacterial intra-ocular infection is present, and the evidence so far available suggests that penicillin, like the sulphonamides, is of little or no use in treatment.

In intra-ocular syphilis, the value of penicillin is still *sub judice*. Interstitial keratitis does not seem to be influenced by it, but there is still some doubt as to whether this condition is spirochætal in origin or not. The uveitis occurring in the secondary stage of syphilis, however, apparently responds well to systemic therapy (Klauder and Dublin, 1946).

CHEMOTHERAPY AND OPHTHALMIA NEONATORUM

The promise of the sulphonamides and penicillin in the treatment of ophthalmia neonatorum has not been belied by experience. Their advent has revolutionized the treatment of the disease, although this by no means indicates that prophylaxis is not still the first line of defence, and is of paramount importance.

It is still commonly assumed that severe ophthalmia neonatorum is predominantly gonorrhœal, but a recent statistical survey (Sorsby, 1945b)

ADVANCES IN OPHTHALMOLOGY

By A. J. B. GOLDSMITH, M.B., F.R.C.S.

Assistant Ophthalmic Surgeon, Middlesex Hospital; Surgeon, Central London Ophthalmic Hospital.

CHEMOTHERAPY: PENICILLIN

PENICILLIN has been discussed in previous reports in this series, but as it is now more freely available it may be of interest to summarize current views on its value and limitations in ophthalmic work in the light of the many clinical and experimental data which have been published during the past year.

Experimental.—The effect of penicillin depends upon its concentration in the tissues, and much has been done in assessing the therapeutic levels in ocular structures provided by different methods of administration. In general, it may be said that intramuscular or intravenous injections give good or adequate concentrations in the lids, conjunctiva, and extra-ocular structures generally, but negligible amounts appear in the aqueous or vitreous fluids of the normal eye, even after massive dosage. Satisfactory penicillin levels can be obtained and maintained in both external and internal ocular tissues by suitable methods of local administration in which the amount of the drug used is much smaller, and which inflict much less discomfort on the patient. For infections of the eye and lids therefore, although not of the orbit, systemic injections are wasteful and unnecessary.

Local administration can be made in the form of drops, lamellæ, creams, crystals or injections, the last either subconjunctivally or into the eye itself. Drops containing up to 2,500 Oxford units per c.cm. in normal saline are well tolerated, but have the disadvantages that the penicillin is labile and that they have to be kept in a refrigerator. Lamellæ of up to 250 units are made with a gelatin or lactose base. The latter are more soluble, but are deliquescent and must be kept in an airtight container. Lamellæ are more stable than drops, but they tend to irritate the conjunctiva, causing a reflex flow of tears which may wash out the penicillin as it dissolves. Creams containing 1,000 units per gramme or more are probably the most satisfactory for domiciliary use. With a suitable base for the cream, potency will be retained even at room temperature for three weeks or more, and they have the additional advantages of being non-irritating and less readily diluted and washed out of the eye by any reflex flow of tears. Finally, among surface methods of application, crystals of sodium penicillin have been used in the treatment of corneal ulcers, the crystals being rubbed into the floor and spreading edge with a spatula (Juler and Johnson, 1946).

These methods give bactericidal levels of penicillin in the lids, conjunctiva and cornea, but with none of them do more than minute amounts

enter the eye itself. In man, subconjunctival injections of up to 500 units are well tolerated and give satisfactory and well-sustained levels in both aqueous and vitreous fluids. In desperate cases of intra-ocular infection, injections can be made into the anterior chamber or into the vitreous cavity. The amount that can be so injected seems to depend upon the purity of the specimen used; the drug does not readily diffuse out of the eye, and aqueous and vitreous concentrations remain high for several hours (Sorsby, 1945a, for references to experimental work).

Clinical.—Ulcerative blepharitis, acute and subacute conjunctivitis and infective corneal ulcers respond well to penicillin, and most of the bacteria found in such conditions seem to be sensitive. The time taken for cure varies, the more chronic diseases, such as blepharitis, may take some weeks. The frequency of application should vary directly with the severity of the infection but should not be less than three times daily. Chronic conjunctivitis, in which the infective element is less important and the symptoms are due more to vascular congestion, glandular hyperactivity, or allergy, responds poorly or not at all. Some few cases of acute conjunctivitis prove resistant and some relapse after initial cure (Brown, 1946; Fraser and Scott, 1946).

With intra-ocular inflammations, it is necessary to differentiate clearly whether they be due on the one hand to bacterial infections, or on the other to circulating toxins or allergens. The first group includes post-operative and wound infections and the metastatic endophthalmitis occurring in meningitis, measles or other exanthemas. These cases may respond well to penicillin if it be used sufficiently early; it is best given by subconjunctival or intra-ocular injection (Mann, 1946a).

Into the second group fall cases of acute and recurrent iritis, iridocyclitis, and choroiditis. In these no bacterial intra-ocular infection is present, and the evidence so far available suggests that penicillin, like the sulphonamides, is of little or no use in treatment.

In intra-ocular syphilis, the value of penicillin is still *sub judice*. Interstitial keratitis does not seem to be influenced by it, but there is still some doubt as to whether this condition is spirochætal in origin or not. The uveitis occurring in the secondary stage of syphilis, however, apparently responds well to systemic therapy (Klauder and Dublin, 1946).

CHEMOTHERAPY AND OPHTHALMIA NEONATORUM

The promise of the sulphonamides and penicillin in the treatment of ophthalmia neonatorum has not been belied by experience. Their advent has revolutionized the treatment of the disease, although this by no means indicates that prophylaxis is not still the first line of defence, and is of paramount importance.

It is still commonly assumed that severe ophthalmia neonatorum is predominantly gonorrhœal, but a recent statistical survey (Sorsby, 1945b)

of the cases at White Oak L.C.C. Hospital brings out the interesting point that the gonococcus is found in only some 25 per cent., the rest being due to infection by staphylococci (35 per cent.), other cocci, various bacilli, and viruses (10 per cent.). The findings emphasize the importance of antenatal treatment of maternal leucorrhœa, whether or not it be of gonorrhœal origin.

The same survey suggests that conjunctival disinfectants should be used in the new-born infant. The best are silver nitrate, 1 per cent., and argyrol, 5 to 20 per cent. If silver nitrate be used it will be safer and more stable if put up in suitable containers, such as paraffin-lined beeswax capsules.

In *treatment of the established disease*, the results given by the local use of penicillin are almost as strikingly superior to sulphonamide therapy as was this in turn to the classical methods. In penicillin therapy no irrigations are given and atropine is used only if the cornea is roughened or ulcerated. Drops, 2,500 units per c.cm., are instilled into the conjunctival sac every five minutes until the discharge ceases; this usually takes one-half to three hours. Thereafter the drops are applied at gradually increasing intervals for two to three days. The routine is exacting but is rapid and free from the disadvantages of systemic medication. All causative organisms, including the virus of inclusion blenorrhœa, appear to be susceptible, and relapses are rare.

Failing penicillin, and in the rare resistant cases, recourse may be had to the sulphonamides. Their local application is quite useless. The most suitable of the group is probably sulphamezathine, of which 0.25 gm. crushed in water or milk is given as an initial dose, 0.125 gm. being given thereafter four-hourly day and night, until forty-eight hours after clinical cure.

Local treatment to the eye is also necessary, irrigations with normal saline and the use of drops of paraffin and atropine, the former to prevent the lids sticking together, the latter in case of involvement of the cornea. About 16 per cent. of cases prove resistant to sulphamezathine, but may improve if a different drug of the series be used.

SYNTHETIC MYDRIATICS

Many patients with eye affections have to use atropine locally for prolonged periods, and a proportion of these develop a sensitization reaction, atropine irritation, with a moist eczema of the lids and face. Apart from the discomfort caused, the resulting swelling of the lids may make it difficult to separate them for necessary inspection and treatment of the eye. The condition subsides on withdrawal of the drug but recurs with any subsequent local use. The alternative natural mydriatics, hyoscine, duboisine, or eumydrine can be given, but as a rule similar sensitization reactions develop with each in turn.

During the war it was feared that a shortage of the natural mydriatics

might develop, and a series of synthetic preparations was tested. It has been reported that one of these, lachesine, or E3, is of great clinical value (Riddell, 1946; Mann, 1946b). Its action is weaker than that of atropine, but it can be used more frequently, apparently without risk of irritation, and it does not give rise to toxic symptoms. It seems advisable that it should be given to those patients in whom mydriatics have to be used for long periods. The stronger atropine can then be reserved, with less risk of irritation, for those occasions when a more powerful effect is necessary, as, for example, to break down adhesions between the pupil margin and the lens.

CONGENITAL CATARACT AFTER MATERNAL RUBELLA

Additions to the nosological list may be looked upon as advances in a negative sense only, but one condition cannot be overlooked in this survey. This is the congenital cataract occurring as a complication of maternal rubella during pregnancy, to which attention was first drawn in Australia (Gregg, 1941). During the past few years several cases have been recorded (Swan, 1944; Long and Danielson, 1945; Prendergast, 1946). The danger period is the first three months of pregnancy: it is said that with German measles in the first six weeks 100 per cent. of babies show cataracts, and that from the seventh to the twelfth weeks the incidence is 50 per cent. Pathologically it is found that the nucleus of the lens which develops during this period is necrotic, and it is thought that the cause of the cataract is a virus infection of the epithelium of the developing lens vesicle. Other ocular defects, glaucoma and microphthalmos, are also seen, and congenital morbus cordis is found in many of the cases. The danger of eye or heart disease in the infant seems to be so great that it has been suggested that maternal rubella during the first three months of pregnancy should be considered as an indication for therapeutic abortion.

It will be remembered that macular vision is not present at birth, but develops during the first few months of life. The eyes of the new-born baby wander vaguely about; they begin to fix objects steadily as the macular area begins to function. Anything which impedes the formation of clear retinal images during the first few months of life prevents the normal development of macular fixation; the irregular movements of the baby's eyes becomes perpetuated as a searching nystagmus, and whatever measures may be taken after the age of six months the nystagmus will persist and visual acuity will always be poor.

The importance of early diagnosis and treatment of this complication are therefore manifest, and it should be borne in mind whenever the mother has had German measles during pregnancy. Even with early and successful operation it is improbable that anything like normal vision will be obtained, but such operation offers the only chance of palliating a permanent and most serious visual handicap.

ORTHOPTIC TRAINING AND THE TREATMENT OF SQUINT

Orthoptic training has now been practised for many years, chiefly in departments attached to the larger eye hospitals. It has been much used during the war, particularly in the treatment of cases of latent squint in the Royal Air Force, and as an adjunct to operation in cases of paralytic and non-paralytic squint. It is generally agreed that the results, cosmetic and functional, of the treatment of squint, have been greatly improved with its help and, although it cannot be looked upon as an innovation, it may be of interest to try to give a picture of its place in the management of the case of strabismus.

Preliminary treatment of squint.—It is still all too common for the oculist not to see the squinting child until the condition has become fixed and one eye has become partially amblyopic. There is fortunately, however, a growing scepticism of the comforting but fallacious advice that the squint is associated with teeth cutting or minor ailments, and that the child will "grow out of it", and many more children are now seen in the stage when the deviation is only intermittently present, and when perfect cosmetic and functional cure can, in a proportion of cases, be achieved simply by the prescription and constant wearing of suitable spectacles. The rationale behind this line of treatment is that the underlying cause of the squint in the first place is a combination of weak fusion of the two ocular images and an imbalance in the accommodation-convergence ratio. As regards the latter factor, the child who is long-sighted has to accommodate in order to see clearly, even in the distance; accommodation is normally accompanied by convergence; if his fusion sense be good, he will learn to accommodate without converging; if it be poor, sooner or later, and often after an illness such as measles or whooping-cough, the normal convergence-accommodation ratio will take charge, and while one eye accommodates in order to see clearly in the distance, the other will converge to an appropriate amount. In order to prevent diplopia, images from the squinting eye will be mentally suppressed, and the eye will become amblyopic. If now, in the very early stage of squint, all long sight be corrected with spectacles, the eyes are put into the normal condition as regards the convergence-accommodation ratio, and with even a weak fusion sense binocular vision will be re-established and functional and cosmetic cure will follow, provided the case be treated early enough.

Whilst this explanation is true of the majority of cases, it does not, of course, hold good for those in which there is a paralytic element, nor for the psychological case, nor for those in which there is some impediment to the formation of clear macular images. All such require more specialized lines of treatment.

In *the neglected case*, as has been said, images from the squinting eye are mentally suppressed and the eye becomes amblyopic; in other words,

although structurally normal its visual acuity is poor. The first step in the treatment of such a case is to correct fully any refractive error that may be present. After this the good eye should be occluded completely, a measure which will improve the visual acuity of the squinting eye fairly rapidly in young children, but much more slowly after the age of eight. After twelve, occlusion is of little value, and as a rule educational considerations militate against the prolonged total occlusion without which it is, at that age, quite useless.

Orthoptic training.—Having once achieved normal or practically normal vision in each eye, either can be used with equal facility, but the squint will still be present. It will now be alternating: when one eye fixes, the other will turn in, and the images from whichever eye deviates will be mentally suppressed to prevent diplopia. It is at this stage that orthoptic treatment can be started, although it is usually unwise to embark upon it before the child is four or five years old, or a permanent antipathy may be caused. The treatment in these cases consists not in the strengthening of muscles, as many assume, but in the redevelopment of normal fusion of the two macular images. This is brought about by the presentation on an amblyoscope, or other suitable machine, of dissimilar but fusible images to the macula of each eye. The first aim is to teach both maculæ to see objects at the same time instead of one macula only functioning while the other is suppressed. Once this simultaneous macular perception has been learned, slides of increasing complexity are used in the machine, teaching first the full fusion of images, and later stereopsis or depth perception. At this stage an attempt may be made to pull the eyes straight. Images are presented to each eye at the angle of squint and fused, and the images are then moved in such a way that the eyes following them and keeping them fused, will become straighter. In some cases, if the squint be small, this will be successful and the patient will be cured.

In most cases, however, operation will be necessary. Once fusion has been learned, the eyes are put mechanically as nearly straight as possible, and orthoptic treatment is continued, now with little or no angle of deviation to overcome. Fusion and stereopsis are developed still further with the eyes now straight on the amblyoscope, and are translated from the machine into everyday life. The last step is not one of great difficulty, as with a well-developed fusion sense the child will easily learn to become conscious of diplopia if the eyes deviate from parallelism, and he will automatically keep the eyes straight to obviate the double vision. In very many cases the eyes will now remain straight whether or not glasses be worn: a considerable cosmetic advantage which is less often obtained by methods of treatment in which orthoptic training is not employed.

To summarize, in the treatment of squint with orthoptic methods the cure achieved is functional as well as cosmetic, and is more likely to be stable and permanent. Operation is not the end-all of treatment but is only a

ORTHOPTIC TRAINING AND THE TREATMENT OF SQUINT

Orthoptic training has now been practised for many years, chiefly in departments attached to the larger eye hospitals. It has been much used during the war, particularly in the treatment of cases of latent squint in the Royal Air Force, and as an adjunct to operation in cases of paralytic and non-paralytic squint. It is generally agreed that the results, cosmetic and functional, of the treatment of squint, have been greatly improved with its help and, although it cannot be looked upon as an innovation, it may be of interest to try to give a picture of its place in the management of the case of strabismus.

Preliminary treatment of squint.—It is still all too common for the oculist not to see the squinting child until the condition has become fixed and one eye has become partially amblyopic. There is fortunately, however, a growing scepticism of the comforting but fallacious advice that the squint is associated with teeth cutting or minor ailments, and that the child will "grow out of it", and many more children are now seen in the stage when the deviation is only intermittently present, and when perfect cosmetic and functional cure can, in a proportion of cases, be achieved simply by the prescription and constant wearing of suitable spectacles. The rationale behind this line of treatment is that the underlying cause of the squint in the first place is a combination of weak fusion of the two ocular images and an imbalance in the accommodation-convergence ratio. As regards the latter factor, the child who is long-sighted has to accommodate in order to see clearly, even in the distance; accommodation is normally accompanied by convergence; if his fusion sense be good, he will learn to accommodate without converging; if it be poor, sooner or later, and often after an illness such as measles or whooping-cough, the normal convergence-accommodation ratio will take charge, and while one eye accommodates in order to see clearly in the distance, the other will converge to an appropriate amount. In order to prevent diplopia, images from the squinting eye will be mentally suppressed, and the eye will become amblyopic. If now, in the very early stage of squint, all long sight be corrected with spectacles, the eyes are put into the normal condition as regards the convergence-accommodation ratio, and with even a weak fusion sense binocular vision will be re-established and functional and cosmetic cure will follow, provided the case be treated early enough.

Whilst this explanation is true of the majority of cases, it does not, of course, hold good for those in which there is a paralytic element, nor for the psychological case, nor for those in which there is some impediment to the formation of clear macular images. All such require more specialized lines of treatment.

In *the neglected case*, as has been said, images from the squinting eye are mentally suppressed and the eye becomes amblyopic; in other words,

ADVANCES IN
OTO-RHINO-LARYNGOLOGY
By W. I. DAGGETT, M.B., B.Ch., F.R.C.S.
Surgeon, Ear, Nose and Throat Department, King's College Hospital.

CHEMOTHERAPY IN AURAL SUPPURATION

THE SULPHONAMIDES.—Two years ago Watkyn Thomas (1944) wrote about the use and abuse of sulphonamides in aural suppuration. He then issued a timely warning against indiscriminate use of such drugs and mentioned pitfalls which might be encountered if case selection were faulty or dosage wrongly assessed. The conclusions he came to are as sound to-day as they were then. Since this article appeared there has been a cleavage of opinion between those, chiefly otologists, who maintain that sulphonamides should with few exceptions be withheld and those who favour giving these drugs to every patient suffering from acute otitis media. The reasons for this fundamental difference of opinion are not far to seek. Otologists too frequently see patients seriously ill but almost symptomless after sulphonamides have been given: they are also confronted, although less frequently, with cases in which inflammatory symptoms have completely subsided and yet a severe degree of permanent middle-ear deafness remains (Ewart Martin, 1944). On the other hand, many practitioners confidently assert that since the advent of the sulphonamides the number of patients requiring the cortical mastoid operation has been reduced in a miraculous way. This is an impression unsupported by figures, and statistics collected would be fallacious, for even before the advent of sulphonamides there was a big year-to-year variability in the incidence of acute mastoiditis (Ormerod, 1944). There is little doubt that medical men have at their disposal a drug which in early acute otitis media quickly relieves pain, restores the well-being of patients, and in a high proportion of cases attains the desired effect, namely, restoration of normal function.

In order to clarify an issue which has become unnecessarily involved it is intended first to mention those cases in which sulphonamides are certainly indicated and those from which they should definitely be withheld.

Definite indications.—(1) Acute otitis media with fulminating onset and severe initial general disturbance, in which the drug is aimed at the blood invasion of which the ear condition is only a part. (2) Cases in which complications such as meningitis have supervened. (3) Cases which, as a result of otitis media in the past, have had a dry perforation for years and develop a fresh infection from swimming baths or other causes. (4) Cases in which an acute flare-up occurs on top of a long-standing chronic otitis media. After such a flare-up has subsided, the chronic otitis media must be treated upon its merits, for sulphonamides will not effect a cure.

Definite contraindications.—(1) Cases in which the ear has been discharging for over ten days and progress is unsatisfactory, so that suspicions

stage, and not the most important stage in it. The older lines of treatment by occlusion and operation gave good vision in both eyes, and as a rule good cosmetic results, but such were liable to be less stable, less satisfactory and less permanent. The most important factor in obtaining good results is that the patients should be seen and treated as soon as any deviation, even if transient, is noticed.

Orthoptic training is of value not only in the treatment of squint in children, but also for the heterophoria or latent squint of adults. In this the eyes tend to take up some position other than parallelism and constant muscular effort is necessary to check this and prevent diplopia. Such is commonly productive of symptoms, headaches or eye-aches, blurring of print when reading, or even transient diplopia. In assessing the importance of heterophoria in the causation of these symptoms, regard has also to be paid to the patient's general health, conditions of work, and psychological make-up. In those in whom heterophoria is the chief factor, a short course of orthoptic exercises, on lines somewhat similar to those used in the later stages of squint training in children, may be of great value in toning up the weak muscles. In adults, orthoptics is therefore directed towards strengthening weak muscles, whilst in children its object is to re-educate a lost or maldeveloped capacity for binocular vision.

References

Brown, C. A. (1946): *Brit. J. Ophthal.*, **30**, 146.
Fraser, J. C., and Scott, A. A. B. (1946): *Ibid.*, **30**, 168.
Gregg, N. M. (1941): *Trans. Ophthal. Soc. Austral.*, **3**, 35.
Juler, F. A., and Johnson, G. T. (1946): *Brit. J. Ophthal.*, **30**, 204.
Klauder, J. V., and Dublin, G. J. (1946): *Arch. Ophthal.*, **35**, 384.
Long, J. C., and Danielson, R. W. (1945): *Ibid.*, **34**, 24.
Mann, I. (1946a): *Brit. J. Ophthal.*, **30**, 134.
—— (1946b): *Ibid.*, **30**, 8.
Prendergast, J. J. (1946): *Arch. Ophthal.*, **35**, 39.
Riddell, W. J. B. (1946): *Brit. J. Ophthal.*, **30**, 1.
Sorsby, A. (1945a): *Ibid.*, **29**, 511.
—— (1945b): "Ophthalmia Neonatorum," London.
Swan, C. (1944): *J. Path. Bact.*, **51**, 289.

Penicillin.—Evidence suggests that in future penicillin will be used with fewer qualms than the sulphonamides in the treatment of acute otitis media, but masking of symptoms may still occur. Surgical acute mastoiditis never has resolved because sulphonamides were given, but reports have already been published describing such cases which recovered without operation when treated with penicillin. Allman (1945) quoted twenty-seven cases of scarlet fever mastoiditis cured without surgery. Macbeth (1946) described cases with acute mastoiditis but intracranial complications so grave that immediate operation was deemed too hazardous. Penicillin was being given to these patients and mastoidectomy was contemplated when the general condition improved. During treatment, local signs and symptoms disappeared, X-rays cleared, and recovery took place without further interference. Much more experimental work is necessary before penicillin can become an accepted treatment which can replace surgery. At present operation must be looked upon as the only safe procedure and penicillin as an adjuvant. Undoubtedly otologists can now choose their time for surgical intervention, they need no longer exhaust themselves and their theatre staffs by insisting on midnight emergency operations.

AFTER-TREATMENT OF THE CORTICAL MASTOID OPERATION

One of the greatest strides in otology has been in the after-treatment of cortical mastoid cavities. Painful dressings spread over a period of weeks. are a thing of the past. If the cortical mastoid operation has been efficiently performed, the cavity can be freely dusted with sulphanilamide 1 part, sulphathiazole 3 parts and then closed completely. Many surgeons put in a narrow rubber-glove drain for twenty-four hours, but this makes little difference to healing, which is usually complete in a week. It is rare for the clot which forms to break down, but if this should happen the lower part of the wound can be opened without trouble. Excellent results have also been described by Macbeth (1945), who, following the ideas of the Floreys, stitched up but allowed room for small tubes through which penicillin could be regularly instilled. A better plan is that of Reading (1946) which makes no demands upon the nursing staff: the cavity is filled with plasma in which penicillin has been dissolved, thrombin is added so that the plasma is converted into a firm jelly-like clot, and the wound is then completely stitched.

DEAFNESS

Since an optimistic article concerning the operative treatment of deafness appeared in a widely circulated periodical, medical men have been constantly questioned by their deaf patients about prospects of cure. From the outset it must be clearly understood that the operation in question is only performed for some cases of otosclerosis and that its scope does not include perception (internal ear) deafness of any kind. Thus sufferers from senile deafness or gunfire deafness cannot hope to benefit.

of impending mastoiditis are aroused. At this stage it is far too late for sulphonamides to be effective, moreover to give them means that signs and symptoms will be masked. In any case it is undesirable to begin sulphonamide treatment later than the first twenty-four hours after onset.

(2) Simple uncomplicated chronic otitis media.

When it is decided to give the sulphonamides, all the well-known principles must be observed. To be effective they must be given early and in full doses, whilst a careful watch must be kept on fluid intake, urine output, and blood picture. Treatment should continue until the temperature has been normal for forty-eight hours, but if there has not been a good response after six days, failure must be admitted and the drug stopped.

It remains now to clarify the attitude towards the average case of acute otitis media with sudden onset and only moderate general disturbance. In the early stages the drum is congested but not bulging, landmarks are clearly defined, whilst hearing remains good. Myringotomy at this stage is not indicated, but within twelve to twenty-four hours the drum may bulge, and deafness may become obvious: myringotomy now becomes necessary. Many otologists treating such patients in hospital prefer to withhold sulphonamides. They know that many in the congestive stage get well if put to bed and left alone. They are content to watch because, should congestion progress to suppuration, they can perform myringotomy without delay. They also know that when sulphonamides are given in this initial period, although most cases will resolve rapidly, some few may progress to suppuration in a most insidious way. Earache may disappear and the only evidence may be a lustreless drum and deafness.

Although otologists, believing that delayed myringotomy may in some cases account for deafness, often prefer to withhold sulphonamides from patients under their own constant observation, practitioners are justified in prescribing these drugs in the earliest stages of acute otitis media *provided they are alive to two danger periods*. The first danger period occurs within two to three days, when myringotomy may be necessary although a lustreless drum and deafness are the only guides. The second is after the second week, when mastoiditis requiring operation may develop with so few signs that even experienced otologists will be assailed with doubts. If any case treated with sulphonamides continues to discharge during the third week, suspicion should be aroused, and if in addition marked deafness is present, mastoid involvement is almost certain, even if no other signs exist. In this second danger period occasional cases of mastoiditis occur in which even discharge is absent and the only evidence may be a thickened drum and marked deafness. Serial X-rays taken at three-day intervals will often help to elucidate difficult cases. In short practitioners who give sulphonamides at the onset have the satisfaction of alleviating symptoms, calming the fears of anxious relatives, and seeing a high proportion of their patients getting perfectly well. If their vigilance is redoubled during the danger periods. they may safely avail themselves of these advantages.

MÉNIÈRE'S DISEASE

Considerable attention has been given in recent years to the treatment of Ménière's disease. It is now believed that the endolymph spaces are overloaded with fluid and that symptoms become apparent if one labyrinth is affected to a greater extent than the other. Ordinary tests are not often delicate enough to assess accurately the loss of cochlear and vestibular function, but modern audiometry combined with the differential caloric tests elaborated by Cawthorne, Fitzgerald and Hallpike (1942) have put the diagnosis on a sure footing. A unilateral vestibular preponderance of function can now be detected.

Medical treatment must always be given a prolonged trial before surgical measures are contemplated and the most successful line of medical treatment is based upon the theory of Dederding (1929) that a general condition of fluid retention exists as a result of faulty water metabolism. Fluid intake must be rigorously restricted to 2½ pints a day, whilst salty foods, such as tinned, cured, smoked and otherwise preserved meat and fish, tinned soups, and most proprietary breakfast cereals, must be forbidden, a minimum of salt must be used in preparing food and no salt whatever added at meals. It is. surprising how often these most exacting and unpleasant restrictions reduce the number and severity of attacks; particularly is this so when patients are naturally big tea or beer drinkers and normally add excessive salt to their food. Sedatives, such as phenobarbitone, ½ grain (32 mgm.) t.d.s., can be given concurrently.

Recently, there has been considerable enthusiasm for the use of histamine, or alternatively nicotinic acid if patients are found to be insensitive to the former. The results obtained in this country have been less encouraging than those claimed by Miles Atkinson (1943). As an adjuvant to fluid and salt restrictions these drugs may be useful, but their administration is somewhat complicated and treatment is usually·carried out in hospital. Maintenance doses have to be carried on for so long that patients often lose heart. The mode of action of these drugs is obscure even if, as Williams (1946) contends, hydrops of the endolymph spaces is an allergic manifestation. Histamine is first given intravenously: 1.9 mgm. of histamine acid phosphate in 250 c.cm. of normal saline is run in at the rate of 60 drops a ·minute. After two or three treatments at daily intervals, a subcutaneous maintenance dose of 0.1 to 0.2 mgm. histamine base is given thrice weekly.

Nicotinic acid is usually given intramuscularly at two-day intervals, beginning with 25 mgm. and working up to 100 mgm., according to tolerance. An attempt is then made to change to oral therapy, the dosage being 50 mgm. thrice daily on an empty stomach.

Wright (1938a) has found that many patients obtain relief from symptoms when a focus of sepsis is found and eradicated. Fewer otologists now believe that focal sepsis plays an important part in the causation of Ménière's disease; nevertheless, obvious septic foci are better removed·

The operation is called *fenestration* because a small opening is made in the dense bone of the labyrinthine capsule. For years it has been known that decompressing the perilymph spaces in this manner gives rise to dramatic, although temporary, increase in hearing. Subsequent deterioration has been assumed to result from healing of the operative fistula by bone or rigid scar tissue. Otologists have been constantly elaborating their technique hoping that the fistula could be closed by a resilient membrane. It is out of place in this article to describe modern technique but fuller details can be gleaned from the publications of Lempert (1945), Shambaugh (1945) and Simpson Hall (1944). Suffice to say that the present-day operation requires skill and practice which the majority of British otologists have not had the opportunity of acquiring during the busy war years. Many of the biggest hospitals have not in their possession binocular dissecting microscopes, and other special equipment which is essential for the attainment of good results.

Although the operation is being performed in this country, few surgeons have done more than 50 cases, whereas in America there are men who virtually devote all their time to fenestration and can speak of results in over 1,000 cases. It is conceded by all those with most experience that their percentage of successful results was low until they had done at least 50 cases and that even now they have not reached finality regarding technique; wherefore time must elapse before practitioners can confidently urge patients to undergo operation. Provided a surgeon is chosen who has attained the necessary experience it is probable that 50 to 60 per cent. of suitable cases will show worth-while improvement in hearing, perhaps 30 per cent. will hear better but not well enough, whilst 10 per cent. will show no improvement. Only an occasional patient will become more deaf.

Case selection is of the utmost importance and only an otologist should be asked to assess suitability. Generally speaking, unsuitable cases are those over forty, those whose hearing by bone conduction has deteriorated, and those whose hearing for high pitch tones has begun to fall away. Because a post-operative increase of 25 decibels is considered good, those whose hearing in the speech frequencies has already dropped below a 45 decibel loss will be disappointed; they will be improved but they will still be too deaf to appreciate church services or a cinema. Those who are likely to get the most satisfactory results from operation are patients who benefit most from the use of an efficient instrument. Thus it is quite logical to advise young otosclerotics to purchase a suitable aid. In five years' time they will still be young enough to benefit from operation, and by then there will be more finality about technique and greater knowledge about prospects of lasting improvement. Usually the patient who thinks he should have an operation because his instrument is so little help is either using a bad instrument or is an unsuitable case for operation. Reputable deaf aids are now extremely efficient and it is the practitioner's first duty to make sure that his patient is not using a faulty or badly designed instrument.

as has been amply demonstrated by Priest (1945) and others. Systemic chemotherapy instituted early in the treatment of acute osteomyelitis of the frontal bone has saved many lives. Before the advent of the sulphonamides and penicillin this dreaded complication of sinusitis had a high mortality.

HYPERPLASIA OF LYMPHOID TISSUE IN THE POST-NASAL SPACE

Crowe and Baylor (1939) published some interesting observations on treatment of children whose deafness was caused by Eustachian tube blockage secondary to adenoid vegetations. Many of these children had had their adenoids surgically removed on more than one occasion and yet lymphoid tissue persisted in the lateral pharyngeal recesses around the tubal orifices. This lymphoid hypertrophy was treated by radium applications, and subsequent to irradiation the affected area became smooth, the tube again became patent, and hearing improved.

Radon therapy.—During the recent war similar methods were applied to air crew personnel who suffered ill-effects as a result of sudden alteration of barometric pressure (otitic barotrauma). Such men were often found to have lymphoid hyperplasia in, or closely around, the Eustachian tube orifice, giving rise to subacute tubal blockage. Fowler (1944) reviewed the results of treatment amongst American Air Force personnel and found that 79 per cent. went back to full flying duty. Capsules of radon (75 m.c.) were applied upon special wire applicators against each tubal orifice and left in position for twenty-six minutes. Four to six treatments were given at intervals of six weeks. Similar results have been obtained by the accurate focusing of deep X-rays. In peace-time medicine there is scope for irradiation in the treatment of those unfortunate patients whose adenoids have been removed more than once and who yet have symptoms because lymphoid tissue persists in the post-nasal space. Such patients are usually older children who suffer from intermittent deafness and nasal discharge. It is well known that further attempts to remove such lymphoid tissue are doomed to failure: an adenoid curette, however sharp, will glide over the surface, whilst a La Force adenotome fails to include the offending patches.

ACUTE INFECTION OF MOUTH AND THROAT

MacGregor and Long (1944) used penicillin pastilles containing 500 units in a gelatin base in the treatment of Vincent's angina and hæmolytic streptococcal tonsillitis and showed that a useful concentration of penicillin in the saliva could thus be maintained. It has now become an established method of treatment for Vincent's angina to make patients retain such pastilles in the mouth during waking hours; in severe cases systemic penicillin is also given. The results of treatment are excellent, although it is as essential as ever to institute dental surveillance in order to eliminate gum pockets and guard against recurrence. Acute hæmolytic streptococcal tonsillitis responds clinically to penicillin pastilles, but when the infection

Surgical intervention.—Some 20 per cent. of patients fail to improve with medical treatment and upon these, operations planned to destroy labyrinthine function are undertaken with encouraging results. Section of the vestibular branch of the eighth nerve (Dandy's operation) is still practised but with less success than in the hands of the originator. A simple safe procedure is to fenestrate the bony external semicircular canal on the affected side and to destroy the membranous canal by tearing it, removing it, or applying alcohol. Some, following Wright (1938b), inject alcohol through the tympanic membrane and footplate of the stapes. As all these operations, except accurate division of the vestibular branch of the eighth nerve, permanently destroy hearing, the function of the better ear must be taken into consideration before advising surgical treatment. Cawthorne (1943) has rightly pointed out that attempts to conserve hearing function on the affected side are mistaken, because any residual hearing is so distorted that it is actually distressing to the patient.

Cawthorne and Cooksey (1946) have proved the value of exercises which encourage patients to adjust themselves to sudden movements. The best results are obtained when such exercises are begun before operation and continued until post-operative compensation is complete.

PARANASAL SINUSITIS

In the treatment of acute or subacute sinusitis, local treatment with the sulphonamides has proved a failure. Berdal (1945) has shown that a 10 per cent. suspension of sulphathiazole introduced into an infected antrum is without therapeutic effect, whatever the causal organism. In his series there was no reduction in the number of punctures required to clear up the condition, nor was there reduction in the percentage of cases which eventually required operation.

Penicillin, on the other hand, has its uses. When the causal organism is sensitive, introduction of penicillin into an antrum may be successful. There are, however, technical difficulties because the drug in aqueous solution does not remain in the cavity long enough to be effective, and constant replacement is necessary. Trial has been made of a suspension in tragacanth and promising results are sometimes obtained. The most logical method is to introduce a ureteric catheter through an antrum cannula, the latter being withdrawn so that the catheter remains *in situ.* The catheter is then strapped to the cheek and penicillin is introduced at regular four-hourly intervals. The results are good but patients have to be in hospital for treatment, and therefore the advantage over repeated punctures is questionable. Penicillin may be used by the displacement method of Proetz (1945) in chronic cases, but those which improve are apt to become as bad as ever as soon as treatment is discontinued. Proetz has pointed out that when penicillin is used as an intranasal application, 250 units per c.cm. of normal saline is tolerated better than stronger solutions. Penicillin is without effect in the treatment of chronic sinusitis associated with bronchiectasis,

RECENT ADVANCES IN ANÆSTHETICS

By R. R. MACINTOSH, D.M., D.A.

AND WILLIAM W. MUSHIN, M.B., D.A.

From the Nuffield Department of Anæsthetics, University of Oxford.

THE RÔLE OF CURARE

THE introduction of curare into anæsthetics has been a dramatic development. Rarely has a drug been given promotion from the experimental stage to everyday clinical use so unexpectedly as curare. Never did a drug have a more evil history to live down, yet at the moment little but its virtues are discussed. After a stagnant period of nearly 100 years as a pharmacological laboratory tool to immobilize the conscious animal, it has suddenly become an anæsthetic necessity. At the moment the spot-light is focused on it in the operating theatres of Canada, the United States, and Britain.

Every second-year medical student learns that curare paralyses striated muscle by acting on the myoneural junction. This property has now been legitimately capitalized by the anæsthetist to abolish that bane of successful surgery, the motor responses of the lightly anæsthetised patient.

It is well to remind ourselves occasionally that perfect operating conditions can be achieved by a wide variety of means; but whatever the means it is inevitable that the patient has to pay some price for being rendered unresponsive to surgical stimuli. It is the job of the anæsthetist to choose the anæsthetic procedure for which the patient has to pay least in the form of physiological and psychological trauma. Consider the problem of abdominal surgery. Perfect operating conditions here consist largely in abolition of the normal muscular responses to the insult of surgical intervention, or, in other words, perfect muscular relaxation. Admirable muscular relaxation can be obtained by deep general anæsthesia alone, but unpleasant post-operative sequelæ are the rule. Spinal analgesia is not without its hazards, and local analgesia in the conscious patient needs considerable practice to ensure success. A combination of light general anæsthesia to keep the patient asleep and local analgesia to abolish the relevant deep reflexes gives excellent results. Perfect operating conditions can be obtained, too, even more simply, by putting the patient lightly to sleep and then giving an intravenous injection of curare. The operating conditions and the incidence of post-operative sequelæ are no better and no worse than those afforded by the judicious combination of local and light general anæsthesia.

Advantages and disadvantages.—An outstanding feature of curare is the ease with which it can be given. In this respect it has something in common with pentothal and similar intravenous anæsthetics. In one way this enhances the value of the drug but at the same time it increases its hazard, since occasionally the inexperienced are tempted to embark on anæsthetic procedures for which they are not fitted by basic training. Therefore it should be emphasized at the outset that curare should be used only by the

has become peritonsillar such treatment is valueless. Peritonsillitis, before the formation of pus, will respond in most cases to either sulphonamides or penicillin, but when once a collection of pus is present there is still no substitute for incision. In the after-treatment of tonsillectomy there is great scope for the use of penicillin pastilles.

EARLY INTRINSIC CARCINOMA OF THE LARYNX

Until recently, those who devoted their time to the development of irradiation therapy were at a disadvantage because the clinical material at their disposal was limited to cases which laryngologists considered unsuitable for surgery. It has hitherto been accepted that early carcinoma involving one cord without limiting its movement should be treated by laryngo-fissure if there was no reason to suspect implication of muscle or cartilage. Laryngo-fissure is an excellent operation and unsatisfactory results must be attributed to faulty technique or poor case selection. Nevertheless, however good may be the result as regards cure, all patients are left with some degree of permanent huskiness. Evidence is beginning to accumulate which shows that early carcinoma of one cord responds so well to irradiation that the percentage of cures may approach that which follows surgery. If in future, prospects of curability are proved equal in the two methods, irradiation which leaves the voice unaltered must replace surgery. As a result of improved technique the hitherto common sequelæ of perichondritis and pain following irradiation are now rare. Even growths which are comparatively radio-insensitive are curable by irradiation.

References

Allman, C. H. (1945): *J. Amer. med. Ass.*, **129**, 109.
Atkinson, M. (1943): *Arch. Oto Laryng.*, **37**, 40 (and other contributions).
Berdal, P. (1945): *Acta Oto-laryng.*, **33**, 245.
Cawthorne, T. (1943): *J. Laryng. Otol.*, **58**,
——, Fitzgerald, G., and Hallpike, C. S. (1942): *Brain*, **65** 138.
——, and Cooksey, F. S. (1946): *Proc. roy. Soc. Med.*, **39**, 270.
Crowe, S. J., and Baylor, J. W. (1939): *J. Amer. med. Ass.*, **112**, 587.
Dederding, D. (1929): *Acta Oto-laryng.*, suppl. 10.
Fowler, E. P., Jun. (1944): *Arch. Oto-laryng.*, **40**, 402.
Hall, I. S. (1944): *Proc. roy. Soc. Med.*, **37**, 737.
Lempert, J. (1945): *Ibid.*, **41**, 1.
Macbeth, R. G. (1945): *J. Laryng. Otol.*, **60**, 16.
—— (1946): *Proc. roy. Soc. Med.* (in the press).
MacGregor, A. B., and Long, D. A. (1944): *Brit. med. J.*, ii, 686.
Martin, G. E. (1944): *Proc. roy. Soc. Med.*, **37**, 746.
Ormerod, F. C. (1944): *Ibid.*, **37**, 750.
Priest, R. E. (1945): *Ann. Oto-rhino-laryng.*, **54**, 787.
Proetz, I. (1945): *Ibid.*, **54**, 94.
Reading, P. (1945): *Lancet*, i, 811.
Shambaugh, G. E., Jun. (1945): *Arch. Oto-laryng.*, **41**, 189.
Watkyn Thomas, F. W. (1944): *The Practitioner*, **153**, 228.
Williams, H. L. (1946): *Proc. Mayo Clin.*, **21**, 58.
Wright, A. J. (1938a): *J. Laryng. Otol.*, **53**, 97.
—— (1938b): *Ibid.*, **53**, 594.

tion. When curare is superimposed upon a light general anæsthetic the muscles are unable to respond, so that there are no signs by which the depth of general anæsthesia can be judged. The patient may even be conscious, yet the only obvious sign of life is that the heart beat continues. In very large doses curare appears to produce unconsciousness; operations have in fact been carried out satisfactorily on the human subject using large doses of intocostrin only. Its value is being assessed, too, in other operations in which troublesome reflexes are not abolished by light anæsthesia. In thoracic operations it prevents the annoying cough response resulting from stimuli in the neighbourhood of the hilum of the lung. Given with pentothal it prevents laryngeal and masseteric spasm, allowing bronchoscopy, laryngoscopy and intubation to be performed. Muscles in protective spasm relax; thus operations for the relief of such diverse conditions as hæmorrhoidectomy and the setting of a fracture are made easy.

ANÆSTHESIA IN RESPIRATORY OBSTRUCTION

It has long been known that there is a particular risk of sudden fatality associated with anæsthesia in a patient suffering from inflammatory swellings in the neck or floor of the mouth. A quinsy, or spreading infection from a wisdom tooth, may lead to some degree of œdema of the glottis and respiratory obstruction. A general anæsthetic, particularly a basal anæsthetic, in these circumstances, is a hazardous undertaking. Chevalier Jackson points out that if obstruction is severe the accessory muscles of respiration are essential to make respiration tolerably efficient. The accessory muscles are under voluntary control and their action is lost with the onset of unconsciousness. An obstructed patient can be anæsthetised with safety only if a good airway is ensured before he is rendered unconscious. Once this is done such a patient tolerates a general anæsthetic as well as anybody else. A clear airway is imperative; the choice or condemnation of any particular anæsthetic drug is of quite secondary importance. The management of the anæsthetic problem is discussed in a recent book (Macintosh and Bannister, 1943).

ARTIFICIAL RESPIRATION

Artificial respiration during an operation presents no problems provided the airway is clear. The reservoir bag (frequently misnamed "rebreathing bag") is filled with oxygen. The bag is then compressed by hand and the oxygen transferred to the lungs. Many alternative means of inflating the lungs with oxygen are available. The problem is not solved so simply, for example, on the river bank or aboard ship, where apparatus is not to hand.

One of our colleagues (E.A.P.) felt that an answer could and should be found to the long disputed question of which is the best best method of artificial respiration. He asked to be anæsthetised to the stage of respiratory arrest. An endotracheal tube was passed and the pulmonary exchange effected by the different methods of artificial respiration recorded. The results show that the exchange from Eve's rocking method (580 c.cm.) exceeds that of Schaefer (340 c.cm.) and Silvester

trained anæsthetist. It should not be used by the occasional anæsthetist in the hope that it will help in a difficulty which should be countered by other means. For instance, we have heard of it being used to overcome abdominal rigidity consequent on some degree of respiratory obstruction: a tragedy was narrowly averted.

Curare has two great *disadvantages*. By the time it produces the desired degree of abdominal muscular relaxation the action of the diaphragm is gravely impaired; in fact it may become temporarily paralysed. A high concentration of oxygen must be given throughout the operation and the anæsthetist must be ready at any time to give artificial respiration. Although this last warning may sound a little ominous to the uninitiated, it must be remembered that the skilled anæsthetist is familar with respiratory arrest deliberately produced for the benefit of the patient, as for example during intrathoracic operations, or to help the surgeon faced with delicate manipulations around the biliary tract. The second disadvantage of curare is that it increases bleeding. This has not been reported by other writers but it has been true in the cases we have done, and in others we have witnessed. The cause is unknown. It is not due to increase of CO_2 consequent on depressed respiration, because the bleeding is unaffected by artificial hyperventilation. It may be due to the action of curare on sympathetic ganglia where the mechanism of impulse transmission is similar to that in striated muscle, or it may be due merely to diminished action of the thoracic pump, coupled with the fact that the cardiac output is unimpaired.

Dosage.—We have used both the available preparations, and consider that 15 mgm. of curarine chloride (Burroughs Wellcome) is approximately equivalent to 5 c.cm. of intocostrin (Squibb), each c.cm. of which contains 20 "units". Speaking generally, 15 mgm. of curarine chloride combined with light general anæsthesia will give admirable relaxation for abdominal surgery in the average patient. Curare is excreted unchanged in the urine and the intensity of effect of any given dose is determined by the depth of the accompanying general anæsthesia. The duration of its action depends upon the dose given, and the robustness of the patient. In a healthy young man the effect may wear off in twenty minutes, whereas a similar dose in a frail old woman necessitated artificial respiration for just over an hour. The treatment for overdose is artificial respiration until spontaneous breathing is adequate. Physostigmine, or the proprietory drug, prostigmin, is the pharmacological antidote. As a result of some animal experiments by Professor J. H. Burn, we have given up to 5 mgm. prostigmin to the curarized human patient with marked effect.

Two other features of curare are worth mentioning: the loss of the signs of anæsthesia and the general anæsthetic effect of large doses. Anæsthetists rely upon certain "signs" to determine how deeply the patient is anæsthetized. These signs are all motor. Thus the movement of a limb, the character of respiration, the closing of an eyelid, are all muscular responses to stimula-

the use of a special mattress which allows the needle to project from the patient's back throughout the operation. It is true that analgesia can be prolonged indefinitely; after the initial dose additional small doses of local anæsthetic are injected whenever the effect shows signs of wearing off. By this means an extensive abdominal intervention can be undertaken with the use of short-acting anæsthetics, but the advantage is not impressive. In this country few abdominal operations last longer than three hours, and analgesia for this time can be ensured by a "one-shot" injection of nupercaine or amethocaine. Even if the analgesia begins to wear off, satisfactory operating conditions are afforded again by small doses of pentothal.

The most convincing argument in favour of continuous spinal analgesia is its use in cases in which the diagnosis of the condition necessitating laparotomy is uncertain, or mistaken. Thus if procaine, which lasts one hour, is given intrathecally for appendicectomy the operation can be continued with small repeated doses of procaine, even though the operation turns out to be a much longer one involving, for example, resection of gut.

CONTINUOUS CAUDAL ANALGESIA IN MIDWIFERY

Caudal analgesia is not new in obstetrics. As a single dose injection, however, its usefulness is limited by the short-lived period of analgesia. In the continuous method of Hingson and Edwards (1942) the needle is left *in situ* throughout labour, and by repeated injections, analgesia is prolonged for as long as required, the longest time in their series being 26½ hours. With characteristic freedom from conservativeness, a number of clinics in America put the method on trial, and the enthusiasm of some stimulated the American daily press to give it wide publicity.

Simple caudal analgesia has been practised for many years for the surgery of the perineum and pelvis. The method, however, has never seriously challenged low spinal analgesia because of the greater difficulty in placing the needle accurately, coupled with the fact that on occasions analgesia is "patchy". To the difficulties of the "single shot" method is added the necessity of lodging the needle for maybe twenty-four hours, and this in a parturient woman and in a site where infection is difficult to guard against. All this adds up to a method which, although very effective when carried out by those skilled in obstetric practice and in the performance of caudal puncture, holds much hazard for the novice in either.

Disadvantages.—From the obstetric point of view, a great disadvantage is the delay in labour which results. Thus, in one report, 70 per cent. of primiparæ required forceps. The anæsthetist, too, faces hazards. Inadvertent spinal injection is an accident with grave potentialities. Prolonged unconsciousness and apnœa necessitating hours of resuscitation have followed such an occurrence, and some of the cases proved fatal. Infection of the epidural space has been reported. Broken needles, not easily removed, have been another bug-bear. Special malleable needles are now used but

(400 c.cm.), but all these were markedly less than inflation of the lungs (970 c.cm.) by mechanical means.

We suggest that attention to general principles, such as the maintenance of a perfectly clear airway, is of more importance than adherence to any particular method. Eve holds that the circulation is maintained by his method better than by others, and figures of oxygen consumption during artificial respiration, so far unpublished, support this view (E. A. Pask, personal communication).

PENTOTHAL: A WARNING

The inadvertent injection of pentothal into an artery instead of a vein has resulted in gangrene and amputation of arm, hand or fingers. This lamentable accident is more frequent than the number of reports in the medical press would indicate, for medical writers rush into print more eagerly with their successes than with their failures. The usual story is that the upper arm is compressed and the injection is given into a conspicuous superficial vessel which subsequently proves to be an aberrant ulnar artery. The danger is avoided by palpating the vessel before pressure is applied to the upper arm. Intra-arterial injection of pentothal causes an immediate intense scalding pain in the forearm and hand. A pause of a few seconds after injecting the first c.cm. of solution will confirm that the needle is not intra-arterial.

STERNAL PUNCTURE

Infusion into the sternal marrow instead of into a vein was first described in 1941. We can confirm its value as a means of introducing fluids, including anæsthetics, into the blood stream. In our opinion its chief value lies in the fact that it is simple to insert the needle into the marrow, and that once *in situ* the needle does not slip out. Its reliability justifies its use in preference to the intravenous route in ophthalmic and other operations when dislodgement of the needle from the vein would interrupt the smooth course of the operation. The outstanding disadvantage is the tendency of a clot to form in the needle unless a free flow of fluid is maintained through it. The danger of perforating both plates of the sternum is obvious. To minimize this risk many sternal needles are made with safety devices, and we have designed a simple needle, the length of which does not exceed $\frac{3}{4}$ of an inch.

CONTINUOUS SPINAL ANALGESIA

This method still enjoys a considerable vogue in North America but has few devotees in this country. It involves technical difficulties or inconveniences which are justified only if the results are better than those afforded by more simple methods. The technique necessitates the use of an unbreakable needle which, because of its malleability, is not easy to insert; the shifting of the patient on to his back with the needle in position; and

convulsions and death is a common belief. Used judiciously intravenous procaine is said to relieve many forms of pain in an effective, prolonged, and safe manner. First used deliberately in 1943 at the Mayo Clinic to relieve the intolerable itching of jaundice, it has proved an effective analgesic for such diverse purposes as the toilet of extensive burns and for severe herpetic pain. In appropriate dosage, unconsciousness and general anæsthesia result, allowing major surgical operations, including abdominal, to be carried out. The after-effects are said to be slight and the method is full of intriguing possibilities. In another sphere intravenous procaine may prove life saving. Grave conditions require heroic measures; emergency states following on pulmonary embolism and status asthmaticus have been relieved by prompt intravenous injection of procaine. The reflexly spastic vessels in the one and the spastic bronchial tree in the other are both relaxed by procaine. In like manner the vascular spasm accompanying angina pectoris and thrombophlebitis, as well as that in injuries of the limbs, are said to be relieved by the intravenous injection of this drug.

Bibliography

Rôle of Curare
Gray, T. C., and Halton J. (1946): *Proc. roy. Soc. Med.*, **39**, 400.
Griffiths, H. R. (1944): *Canad. med. Ass. J.*, **50**, 144.
Whitacre, R. T., and Fisher, A. J. (1945): *Anesthesiology*, **6**, 124.
Anæsthesia in Respiratory Obstruction
Jackson, C., and Jackson, C. L. (1937): "The Larynx and its Diseases", Philadelphia.
Macintosh, R. R., and Bannister, F. B. (1943): "Essentials of General Anæsthesia", 3rd edition, Oxford, p. 268.
Artificial Respiration
Eve, F. C. (1943): *Brit. med. J.*, i, 535.
Macintosh, R. R., and Mushin, W. W. (1946): *Ibid*, i, 908.
Intra-arterial Pentothal
Macintosh, R. R., and Heyworth, P. S. A. (1943): *Lancet*, ii, 571.
Sternal Puncture
Mushin, W. W. (1945): *Proc. roy. Soc. Med.*, **38**, 307.
Tocantius, L. M., and O'Neill, J. F. (1941): *Surg. Gynec. Obstet*, **73**, 281.
Continuous Spinal Analgesia
Lemmon, W. J., and Paschal, C. W. (1940): *Ann. Surg.*, **III**, 141.
Continuous Caudal Analgesia in Midwifery
Galley, A. H., and Peel, J. H. (1944): *Proc. roy. Soc. Med.*, **37**, 680.
Hingson, R., and Edwards, W. (1942): *Anesth. Analg.*, **21**, 301.
Sievers, J. M., and Mousel, L. H. (1943): *J. Amer. med. Ass.*, **122**, 424.
Spinal Analgesia and Hyperthyroidism
Knight, R. T. (1946): *Anesthesiology*, **6**, 225.
Rea, C. E. (1944): *Surgery*, **16**, 731.
Spinal Analgesia and Asepsis
Evans, F. T. (1946): *Proc. roy. Soc. Med.*, **39**, 181.
Intravenous Procaine
Allen, F. M., *et al.* (1946): *Anesth. Analg.*, **25**, 1.
Funck-Brentano., P., Bourdin, J. S., and dos Ghali (1942): *Mem. Acad. chir.*, **68**, 438.
Gordon, R. A. (1943): *Can. med. Ass. J.*, **49**, 478.
Lundy, J. S. (1942); "Clinical Anesthesia", Philadelphia.
Perez, J. Pintos (1944): *Rev. clin. Españ.*, **12**, 191.

these are more difficult to insert. The disadvantages of this method are emphasized to put the novice on his guard, and not to discredit what promises to be a great advance in obstetric analgesia, provided the conditions are suitable, and the patient is in the hands of skilled obstetrician and anæsthetist.

SPINAL ANALGESIA AND HYPERTHYROIDISM

Any suggestion aimed at improving the chances of an operation in a case of thyrotoxicosis, or which holds out any hope of relieving the grave postoperative condition of thyroid crisis, deserves close attention and trial. States of acute thyroid overactivity are believed to originate in excessive adrenal activity. It is stated that a spinal anæsthetic, by paralysing the adrenal gland, greatly improves the patient's chances. Clinical reports confirm with enthusiasm the beneficial results of this line of action. Patients considered unfit for operation and others in whom operation was suspended because of their poor condition, later gave rise to no anxiety when operated on under general anæsthesia preceded by a spinal. The use of spinal analgesia in established thyroid crisis is more convincing. Here the patient is desperately ill and the prognosis bad. The effect of a spinal anæsthetic is stated to be dramatic: pulse rate, temperature and general condition return rapidly to normal.

SPINAL ANALGESIA AND ASEPSIS

In a carefully prepared paper Frankis Evans (1946) argues that headache and more serious sequelæ of spinal analgesia are probably due to sepsis. As Professor Garrod pointed out at the same meeting, infection may not be confirmed unless a very careful bacteriological examination of the cerebrospinal fluid is made. Evans holds that adequate sterilization of syringe and needle is obtained by boiling, and of ampoules by soaking in lysol and spirit. We hold that all instruments and ampoules should be autoclaved. It has been our routine practice for some years to have small drums each containing the equipment for one spinal anæsthetic. The drums are autoclaved (45 minutes at 20 lb.), and the contents remain sterile and untouched until the anæsthetist uses them. In striving for a sound technique the anæsthetist should keep a sense of proportion. It is all very well to advocate sterile gloves and gown for every case; it is just as important to avoid handling the business end of the spinal needle, to prohibit the nurse holding the instrument with a pair of Cheatle forceps straight out of a jam jar of antiseptic of doubtful age and composition, and to avoid splashing the instruments with antiseptic. Provided care and common sense are exercised the risk of infection is negligible; without them the risk is great, as the high incidence of headache and the occasional disaster testify.

INTRAVENOUS PROCAINE

Intravenous procaine apparently has its uses, but of this we have no personal experience. That inadvertent intravenous injection of this drug can cause

In a sense this is true, as it is common at these times, but it does mean that the gland is relatively short of iodine. The longer the thyroid is kept short of iodine the more likely is the goitre to become hyperplastic and nodular. New gland tissue is laid down and the thyroid swelling will persist. In certain cases of simple goitre in later life, hyperthyroidism is likely to supervene, and in my own cases of secondary hyperthyroidism 75 per cent. of the initial simple goitres dated to puberty and the growth period. It is therefore most important to recognize the significance of an early simple thyroid swelling and to supply the deficiency of iodine. If this is done early the gland swelling will recede, an eventuality which is not likely to occur after a year or two and more than one cycle of hyperplasia. In simple goitre there are no signs of disturbed metabolism.

In *hyperthyroidism* there is excess thyroxine production and symptoms of raised metabolism, i.e. heat production in excess of normal. These must be looked for in the presence of loss of weight, hot moist skin, a tendency to sweating under emotional stress and exertion, with evidence of overdriving of the cardiovascular and nervous systems. Loss of weight is not invariable in the early stages, as the raised metabolism may be offset by increased appetite and food intake. Although anxiety is usually responsible for hyperthyroidism it should be noted that the early symptoms are almost always physical—a difference from an anxiety state, in which symptoms are psychological and usually due to misinterpreted emotional reactions. In early hyperthyroidism there may or may not be some enlargement of the gland and eye signs are often present.

A basal metabolism test is a most useful guide if hyperthyroidism is suspected. In early cases, and if the result of such B.M.R. test is doubtful, further help can be obtained from an iodine remission test. In the normal person, the administration of iodine will not lower the basal metabolic rate to any striking extent, but in mild hyperthyroidism a course of iodine for ten days should result in a fall of 15 to 20 per cent. in the B.M.R. A change in the consistency of the gland is also significant. A hyperthyroid enlargement is likely to be soft, fleshy and vascular; and with the administration of iodine it becomes harder and less vascular. This does not occur when iodine is administered in simple goitre. Hardening of the gland with iodine is therefore strongly suggestive of hyperthyroidism.

In *myxœdema* and *hypothyroidism* the essential feature is a lowered metabolism, and there is an insidious slowing up of all mental and physical processes. The lowered metabolism is accompanied by subjective and objective signs of the lowered heat production, i.e., a lowered body temperature: a valuable guide in the presence of suggestive clinical features. A child will come under observation for retardation of mental processes, slow development, or a generally puffy appearance. Myxœdema in adults, on the other hand, is usually so insidious that the condition is probably recognized first by a doctor when the patient reports for some entirely separate condition.

The basal metabolism provides the best guide for confirmation of the

THE EARLY RECOGNITION OF DISEASE
X.—ENDOCRINE DISEASE

By H. GARDINER-HILL, M.D., F.R.C.P.

Physician, St. Thomas's Hospital.

In the main, there are two groups of endocrine glands, i.e., those subserving growth and development and those connected with some particular phase of metabolism. It is with the latter group that this article is concerned. The early recognition of endocrine disease, as with disease elsewhere in the body, depends upon an accurate knowledge of the physiological function of the organ concerned and the symptoms and physical signs which may be expected when its function is disturbed. There may be excessive or deficient production of hormone or enlargement of the gland with tumour formation, with or without disturbance of hormone production. It would be a comparatively simple matter to recognize endocrine disease at an early stage if it were possible to observe the gland concerned and measure its hormone production. Unfortunately, the sites of most glands are inaccessible and knowledge has not reached the point at which hormone production can be measured. Endocrine disease is manifested by symptoms and signs but in the early stages these are often inconspicuous. Fortunately, when suspicions have been aroused, there are other lines of approach by which to establish a diagnosis. First, metabolic tests can be of great value, as, for example, the basal metabolic rate in thyroid disease, and investigations of the blood sugar, serum calcium and phosphorus, and serum sodium and potassium in pancreatic, parathyroid and adrenal disease. Provocative tests form a second line of approach, and here the iodine remission test in hyperthyroidism, sodium chloride withdrawal in hypocortical adrenalism, and the provocative high carbohydrate diet in reactionary hyperinsulinism may be cited. There is a third line of approach in the therapeutic replacement test; i.e., the response of symptoms, signs and metabolic disturbances to appropriate substitution treatment, e.g., the disappearance of myxœdema with the administration of thyroid extract, or of polyuria of posterior lobe pituitary origin with the administration of pituitrin.

THYROID DISEASE

Thyroid disease may result from insufficiency of raw material iodine— simple goitre, or an excess or diminished production of thyroid hormone— hyperthyroidism and myxœdema.

Every *simple enlargement of the gland* should be regarded as of significance, for it means iodine deficiency, relative or absolute. If the thyroid is short of iodine, a compensatory hypertrophy occurs and this may lead later to hyperplasia. Simple thyroid enlargement is liable to occur at times of physiological stress, i.e. puberty, the growth period, pregnancy and so on, and in the past there has been a tendency to consider it as physiological.

In a sense this is true, as it is common at these times, but it does mean that the gland is relatively short of iodine. The longer the thyroid is kept short of iodine the more likely is the goitre to become hyperplastic and nodular. New gland tissue is laid down and the thyroid swelling will persist. In certain cases of simple goitre in later life, hyperthyroidism is likely to supervene, and in my own cases of secondary hyperthyroidism 75 per cent. of the initial simple goitres dated to puberty and the growth period. It is therefore most important to recognize the significance of an early simple thyroid swelling and to supply the deficiency of iodine. If this is done early the gland swelling will recede, an eventuality which is not likely to occur after a year or two and more than one cycle of hyperplasia. In simple goitre there are no signs of disturbed metabolism.

In *hyperthyroidism* there is excess thyroxine production and symptoms of raised metabolism, i.e. heat production in excess of normal. These must be looked for in the presence of loss of weight, hot moist skin, a tendency to sweating under emotional stress and exertion, with evidence of overdriving of the cardiovascular and nervous systems. Loss of weight is not invariable in the early stages, as the raised metabolism may be offset by increased appetite and food intake. Although anxiety is usually responsible for hyperthyroidism it should be noted that the early symptoms are almost always physical—a difference from an anxiety state, in which symptoms are psychological and usually due to misinterpreted emotional reactions. In early hyperthyroidism there may or may not be some enlargement of the gland and eye signs are often present.

A basal metabolism test is a most useful guide if hyperthyroidism is suspected. In early cases, and if the result of such B.M.R. test is doubtful, further help can be obtained from an iodine remission test. In the normal person, the administration of iodine will not lower the basal metabolic rate to any striking extent, but in mild hyperthyroidism a course of iodine for ten days should result in a fall of 15 to 20 per cent. in the B.M.R. A change in the consistency of the gland is also significant. A hyperthyroid enlargement is likely to be soft, fleshy and vascular; and with the administration of iodine it becomes harder and less vascular. This does not occur when iodine is administered in simple goitre. Hardening of the gland with iodine is therefore strongly suggestive of hyperthyroidism.

In *myxœdema* and *hypothyroidism* the essential feature is a lowered metabolism, and there is an insidious slowing up of all mental and physical processes. The lowered metabolism is accompanied by subjective and objective signs of the lowered heat production, i.e., a lowered body temperature: a valuable guide in the presence of suggestive clinical features. A child will come under observation for retardation of mental processes, slow development, or a generally puffy appearance. Myxœdema in adults, on the other hand, is usually so insidious that the condition is probably recognized first by a doctor when the patient reports for some entirely separate condition.

The basal metabolism provides the best guide for confirmation of the

diagnosis but in hypothyroidism it can fall to –25 to –30 per cent. before manifest myxœdema develops. The blood cholesterol is less reliable, as cholesterol metabolism is subject to many influences other than thyroid. A most valuable confirmatory test of thyroid deficiency in child and adult is the therapeutic trial of thyroid extract. Striking changes will occur within a few weeks if dosage is adequate, and the diagnosis will be confirmed.

PARATHYROID DISEASE

The early stages of hyperparathyroidism from an over-functioning adenoma, and of hypoparathyroidism from congenital aplasia, are accompanied by few symptoms and both conditions are difficult to recognize; in fact, they seldom are recognized until well established. Early on, both might be called biochemical syndromes, as the biochemical changes precede clinical symptoms and signs. The function of parathormone is to mobilize calcium from the bones; in hyperparathyroidism the serum calcium is raised and there is an excess excretion of calcium in the urine. In hypoparathyroidism the serum calcium is low and there is an associated hyperphosphatæmia.

In *hyperparathyroidism*, in due course, there is a characteristic decalcification of the skeleton but radiological changes in the early stages are likely to be insignificant. Polyuria may well be the only early symptom, and this is a result of excess calcium excretion, the so-called calcium diabetes. In an unexplained polyuria, hyperparathyroidism should be borne in mind and tests made for calcinuria with other diagnostic measures. In some cases in the early stages, the hypercalcæmia gives rise to gastric symptoms—loss of appetite, nausea and persistent vomiting—but with such symptoms the possibility of hyperparathyroidism is apt to be overlooked. A serum calcium examination will settle the point. In most cases the diagnosis of hyperparathyroidism is only made when skeletal abnormalities are discovered. There is often a remarkable tenderness of the bones which may lead to X-ray examination, or the diagnosis will be made after a spontaneous fracture, the discovery of skeletal deformities or a bone tumour for which X-ray examination is carried out. Muscular hypotonia, usually present, is apt to be masked by the bone tenderness. Sometimes in the early stages, but usually later, urinary tract symptoms occur as a result of excess calcium excretion. This may cause irritation of the kidney from calcium phosphate crystals or calcium phosphate stones. With any such condition the possibility of hyperparathyroidism should be borne in mind and investigations of serum and urinary calcium carried out to establish the diagnosis.

Hypoparathyroidism in its idiopathic form is an extremely rare condition, and hypoparathyroidism is usually encountered clinically as a result of thyroid operations. Significant symptoms—tetany and cramps—are not likely to arise until the serum calcium has fallen to a level of about 6 mgm. per cent., at which point exaggerated neuromuscular irritability will become evident. The irritability of the nervous system may be sufficiently severe to produce epileptic seizures. If latent tetany is suspected, the Trousseau and

Chvostek signs, depending upon exaggerated neuromuscular irritability, will help in the diagnosis, which can be established by the finding of a low serum calcium. In hypoparathyroidism this is associated with hyperphosphatæmia, a combination of biochemical findings of diagnostic significance.

HYPO- AND HYPER-INSULINISM

The early recognition of these conditions is not, as a rule, easy, as there is no direct method of assessing the amount of insulin production.

Hypo-insulinism, i.e. diabetes, may develop explosively or insidiously, the former usually after an acute infection, when failure of recovery, undue fatiguability and loss of weight may be found, with thirst and polyuria. In the insidious form, early symptoms are often inconspicuous, but a gradual deterioration in health, with thirst, polyuria and loss of weight lead to an examination of the urine. In such cases, thirst and polyuria are often first noticed after meals—a reaction to the post-alimentary hyperglycæmia. The excessive quantity of urine results from the kidney having to excrete more water, partly to get rid of the sugar excess and partly owing to the polydipsia.

In early diabetes and hypo-insulinism there are seldom physical signs, but the finding of sugar in the urine leads to investigations of fasting blood sugar and a sugar tolerance test, which will show a typical diabetic curve.

There are two types of *hyper-insulinism*—the reactionary, due to a prolonged and excessive intake of carbohydrate, which leads in certain individuals to a more or less regular excessive production of insulin and symptoms due to hypoglycæmia late after meals, and that due to tumour formation of the islet tissues, in which excessive quantities of insulin are produced at irregular intervals and for no obvious reason.

The clinical symptoms of hyper-insulinism are characteristic and easy to recognize if the condition is borne in mind. Hypoglycæmia produces a hungry sinking feeling in the pit of the stomach with nervousness and apprehension and a feeling of weakness and shakiness of the hands and knees. Dimness of mind and dimness of vision develop subsequently, with palpitation of the heart, sweating and sometimes loss of consciousness and even convulsions. In the reactionary type, these symptoms will be noticed some time after meals which have contained a considerable quantity of carbohydrate. The condition seems to have been more common during and since the war owing, no doubt, to the increased carbohydrate diet many have had to take. In the tumour form, rare, similar symptoms occur irregularly but usually during the night, and at times when there has been long abstinence from food.

The diagnosis depends upon correlating the symptoms of an attack with a low blood sugar. In the reactionary form, a provocative test can be carried out with a high carbohydrate diet and a sugar tolerance examination will give a characteristic result. After a dose of 50 gm. of glucose, the blood sugar will rise to a normal level and then fall gradually or quickly to levels far below the normal. In the tumour type, a sugar tolerance test may be inconclusive

but the correlation of the attacks with low blood sugar levels will show their hypoglycæmic origin. There should not be any difficulty in diagnosing the reactionary form, but a laparotomy may well be necessary to establish the presence of an islet tumour.

CORTICAL ADRENAL DEFICIENCY

Addison's disease usually develops insidiously and it is often only when the characteristic pigmentation appears that the condition is suspected. By this time there has usually been pronounced weakness, lassitude and loss of energy for some months, undue fatiguability on exertion and often sleepiness and lethargy. Such symptoms are, of course, found in a number of conditions, but in Addison's disease, sooner or later, unexplained gastro-intestinal disturbances—anorexia, loss of appetite, nausea and attacks of vomiting with diarrhœa or constipation—occur. Then, on examination, a low blood pressure is found and the significance of the symptoms is recognized. At this point the help of the biochemist should be enlisted to establish the diagnosis. In the absence of adrenal cortical hormone, there is a sodium and chloride leak from the kidneys and an excess of these substances in the urine and, as a result, their level in the blood falls; not invariably, however, in the early stages. Estimations of the urinary and serum sodium and chloride should be undertaken to support the diagnosis. One or other type of provocative test may well be required to establish it. In Addison's disease, a sodium chloride withdrawal test will usually result in an excessive fall in the blood sodium and chloride levels. An alternative plan is to provoke an excessive increase in sodium excretion by administering potassium salts. One or other method will usually make the diagnosis clear.

Finally, as in other endocrine deficiency syndromes, a therapeutic test with cortical hormone will confirm diagnosis, and not only improve symptoms and physical signs but restore the altered blood chemistry to more or less normal. If the cortical lesion is of a progressive nature, this improvement will, of course, be only temporary and not possible to maintain.

POST-PITUITARY HYPOPITUITARISM: DIABETES INSIPIDUS

Thirst and polyuria have been mentioned as characteristic symptoms of diabetes mellitus. Polyuria may also be an early symptom of hyperparathyroidism. Thirst and polyuria are the leading symptoms in post-pituitary deficiency, i.e. diabetes insipidus. In this condition, symptoms as a rule develop suddenly, but that will be determined by the nature of the lesion. There may be destruction of the posterior lobe from an anterior lobe or neighbourhood tumour, in which case tumour symptoms may precede and dominate the clinical picture. Thirst and polyuria, however, of sudden onset and without glycosuria, are highly suggestive of diabetes insipidus and, in the ordinary form, there are seldom noteworthy physical signs.

If diabetes insipidus is suspected, tests of water-salt metabolism should be carried out. It is essential first to correlate water intake and output and

note chloride concentration in specimens of urine. In the absence of the posterior lobe pituitary hormone, the kidney is unable to concentrate chloride, and in diabetes insipidus the polyuria diminishes if salt intake is restricted. To establish the diagnosis of this condition it is useful to carry out a provocative test, a few days with increased salt administration, when the polyuria will increase but urinary chloride will not increase correspondingly. This is then followed by a therapeutic test with pituitrin. If the condition is one of true diabetes insipidus, pituitrin will not only reduce the increased polyuria but increase the urinary chloride concentration in spite of the increased intake of sodium chloride. A provocative test with sodium chloride will distinguish diabetes insipidus from hysterical polydipsia and polyuria. In the latter condition, there is no inability of the kidney to concentrate chloride.

CONCLUSION

These few notes on the early diagnosis of the metabolic group of endocrine disease will show that such diagnosis may often be difficult. There are several reasons for this:—First, the glands concerned, with the exception of the thyroid, are located in inaccessible sites and it is not possible by the ordinary clinical methods to obtain information of the gland's size. Secondly, the body as a whole and the particular systems, nervous, osseous, muscular, in which disturbances of function will occur, seem to be comparatively insensitive to minor disturbances of metabolism. This is appreciated when it is realized that the basal metabolism in hypothyroidism can fall to about −25 to −30 per cent. before disabling myxœdema appears; whereas in hyperthyroidism basal metabolic rate levels of +25 per cent. may be present without any very obvious clinical features of Graves's disease or raised metabolism. Again, in hypoparathyroidism the serum calcium can fall to about 6 mgm. per cent. before manifest tetany develops, and in hypoglycæmia the blood sugar can fall to about 0.05 gm. per cent. before there is any serious disturbance of function in the central nervous system. In hyperparathyroidism and in diabetes mellitus, a serum calcium of 12 mgm. per cent. and a blood sugar of 0.25 gm. per cent. may be unaccompanied by any symptoms directly due to the level. It should again be noted that in the early stages of this group of conditions there is often a remarkable absence of telling physical signs. In fact, in the early stages, these diseases are what might be termed metabolic or biochemical syndromes with disturbances of metabolism, basal or of some particular metabolite—carbohydrate, calcium, sodium—with which the particular endocrine gland is concerned. The onset may be unimpressive, as in diabetes mellitus, hyperparathyroidism and diabetes insipidus; the first sign an increase in water output to facilitate the clearance of sugar, calcium and chloride by the kidney. It is therefore not surprising that in the early stages of such biochemical syndromes the chief help in diagnosis has to be obtained from biochemical tests. These are of great value in confirming suspicions when clinical pointers raise the possibility of this group of diseases.

REVISION CORNER

This section is devoted to short articles in which experts summarize modern treatment and clinical procedures, particularly for the benefit of general practitioners who have returned from the Forces.

THE MALE SEX HORMONE

THE testes are known to produce two hormones, an androgen or substance with a predominantly male activity, and an œstrogen, indistinguishable from the female sex hormone, œstradiol. The former is known as testosterone and is produced by the interstitial cells of Leydig. The latter is probably produced in the seminiferous tubules and is not concerned in this discussion.

PHYSIOLOGICAL ACTIONS

The actions of testosterone have been investigated, both in men and in experimental animals, by the observation of the effects of removal or destruction of the testes and of the effects of the injection of extracts of animal testicles and of synthetic hormones. The physiology of the secretion of testosterone has been studied by observing the effects of removal of the pituitary glands of various animals and of the injection of anterior pituitary extracts and of substances from the blood and urine of pregnant animals, the actions of which closely resemble those of anterior pituitary extracts. *The latter substances are known collectively as gonadotrophins.* There are probably two types: the one, known as follicle-stimulating hormone from its action in females, controls the function of the seminiferous tubules of males; the other, known because of its action in females as the luteinizing hormone, stimulates the interstitial cells of the testes to produce testosterone. Both types of action are manifested by anterior pituitary extracts. The anterior pituitary-like substance obtainable from the serum of pregnant animals (usually mares) is mainly follicle-stimulating, that from the urine (usually human) being mainly luteinizing. The production of gonadotrophin by the pituitary is, in turn, controlled by the testes, being depressed when the concentration of testosterone in the circulating blood is high, although it is probable that the depressant action of testosterone is less than that of the œstrogens. In small doses androgens have themselves a temporary gonadotrophic activity.

The functions of testosterone are to ensure the normal growth and maintenance of the external genitalia, and of the prostate and seminal vesicles. It is responsible for the growth of hair in the normal male distribution, for the lowering of the vocal pitch which occurs at puberty, and for the male configuration of the skeleton and muscles. It has an important effect on emotional reactions, increasing aggressiveness and the sexual urge, although it must be remembered that both these masculine traits are dependent to an even greater extent upon the psychological make-up.

THERAPEUTIC REACTIONS

In some respects, testosterone has an action antagonistic to œstrogens, but by no means in all. Space does not admit of a full discussion of the complicated effects of androgens on the female reproductive organs. However, atrophy of the ovaries is a constant effect of large doses given for a long time. Ovulation is arrested, menstruation inhibited and the endometrium atrophied. Apart from the well-authenticated effects of androgens on the sexual organs of both sexes, a number of other effects have been described. Patients often gain weight while under treatment, owing probably to increased muscular development. The circulation in the extremities may be improved and it has been claimed that androgens have a general vasodilating effect.

They have, however, occasional unwanted effects. In men, large doses produce atrophy of the testes by suppression of the anterior pituitary. In young animals, this may result in failure of testicular descent, and in mature animals there is suppression of spermatogenesis. In women, the pitch of the voice may be lowered, hair grows in a masculine distribution, acne appears on the face and the clitoris enlarges. Fortunately these results are transient and are usually only seen when the dosage is excessive.

<center>INDICATIONS FOR THERAPY</center>

In men, the most important and perhaps the only indication for male hormone therapy is testicular deficiency, the symptoms of which are small external genitals, deficient hair in the male distribution, excessive length of the long bones, a high voice, a female distribution of fat and often feminine psychological traits. Good results have been claimed in peripheral vascular disorders, especially Buerger's disease, and in angina pectoris, but these observations still lack substantiation. In senile enlargement of the prostate, an improvement in symptoms is sometimes observed, probably because of a beneficial action on bladder tone, but there is no reduction in the size of the prostate. Prostatic cancer is made rapidly worse. Except when it is due to testicular deficiency, impotence is unaffected by male hormones, which should be reserved for those cases in which unequivocal evidence of hypogonadism is present. Occasional improvement is, however, seen in the impotence of middle age. Here some caution is advisable, especially with patients who suffer from cardiovascular disease. Death during coitus is not uncommon. Androgens are often prescribed in the hope of curing male sterility. The experimental basis for the treatment is insecure, and no good evidence exists that it is ever effective.

In women, male hormone therapy may be used when it is advisable to stop menstruation, as in the excessive bleeding of metropathia hæmorrhagica and of fibroids. Fibroids often shrink during treatment and so, it has been reported, do endometriomas. In metropathia hæmorrhagica, menstruation, when it returns, may become normal. The symptoms of fibroids eventually recur, but often not for some months after the end of treatment. In other gynæcological conditions, male hormone treatment is still in an experimental stage. In the menopausal syndrome it is effective, but less so than the administration of œstrogens. Similarly, it is less effective in the suppression of lactation. In "chronic mastitis" it is often successful in relieving pain; a result rather hard to explain on experimental grounds.

<center>METHODS OF ADMINISTRATION</center>

Androgenic treatment may be administered by any one of three routes: testosterone propionate by weekly intramuscular injection; methyl testosterone orally, three times a day; or methyl testosterone implanted subcutaneously as pellets. It is difficult to give precise instructions about dosage as this varies greatly with the condition to be treated and the sex and constitution of the patient. Commercial testicular extracts are completely valueless by any route.

<div align="right">RAYMOND GREENE, D.M., M.R.C.P.</div>

ENLARGEMENT OF THE LYMPH NODES

IN disease processes of unknown causation the histological is the only satisfactory basis for classification, and, in this respect, enlargements of lymph nodes fall into three broad groups:—

    (1) The reactive-inflammatory
    (2) The proliferative (reticulosis)
    (3) The neoplastic (reticulosarcoma)

The first group includes those in which the lymph nodes react to a recognized

or presumptive infection or toxic process. The proliferative group is unique; in it, the histological criteria are lacking, although many of the biological attributes of neoplasia are present. There is a progressive proliferation, throughout the reticulo-endothelial system (lympho-reticular tissue), of primitive cells which undergo differentiation to more adult types. This group of reticuloses is divided into follicular and medullary types depending upon the part of the lymph node from which proliferation springs. For example, in Hodgkin's disease the proliferated reticulum cells of the medulla become differentiated to myeloid and fibril-forming elements; thus histologically it is a fibro-myeloid reticulosis of medullary type; similarly, lymphoid leukæmia is a lymphoid medullary reticulosis. A reticulosis may arise as a general or systematized disorder of the lympho-reticular tissue throughout the body, or it may first be manifest as a localized affection of one group of lymph nodes. Much that has been said of the proliferative diseases applies to the neoplastic group, but in the latter the classical features of malignant disease—infiltration and stromal destruction—are present. These tumours are the reticulosarcomas, and a variety of cellular types, corresponding with the derivatives of the primordial mesenchyme, may be recognized. Their initial appearance may be systematized or local.

THE REACTIVE-INFLAMMATORY GROUP

Simple *pyogenic and tuberculous lymphadenitis* usually offers no diagnostic problem; but there are instances, particularly of generalized tuberculous lymphadenitis, when biopsy is required. Doubts will usually be resolved by a period of observation of four to six weeks. It is worth recalling that Hodgkin's disease has been observed to arise in a group of lymph nodes already enlarged from draining an infected area.

Glandular fever is usually diagnosed readily once suspicion is aroused. Tonsillitis with enlargement of lymph nodes other than those draining the tonsil; unexplained lymphadenitis with fever and perhaps a rash; abdominal pain or jaundice with enlarged superficial lymph nodes are some of the guises of this pleomorphic disorder. Confirmation is given by the differential leucocyte count and the Paul-Bunnell reaction.

The Still-Felty syndrome of rheumatoid arthritis with lymph node and splenic enlargement is easily recognizable; it is accompanied in some cases by thrombo-cytopenia and a hæmorrhagic tendency, in others by a leucopenia.

In children and adolescents, generalized enlargement of lymph nodes and splenomegaly is a common response to many infections. At times they follow a mild febrile attack of obscure cause, when moderate lymph node enlargement may persist for several months. The histological changes are of a "*non-specific reactive hyperplasia*", the blood count is normal, and general health is unaffected; with the passage of time the lymph nodes become impalpable.

It is probable that the *sarcoidosis of Boeck* should be included in this group, for there is at least indirect evidence of its tuberculous origin. The clinical picture is complex, being compounded of the following: skin lesions, either the red-brown plaques of miliary lupoid, or the violet infiltration of the butterfly area, called lupus pernio; enlargement of lymph nodes; splenomegaly; an indolent irido-cyclitis; enlargement of the parotid and lachrymal glands; a miliary infiltration of the lungs; and lesions in the carpal phalanges, causing spindle-shaped deformity of the fingers. Any of these may appear first, and the disease runs a protracted course which may extend over twenty-five years: individual lesions resolving, to be followed by the appearance of others. The miliary infiltration of the lungs disappears to leave fibrosis; the intractable irido-cyclitis often leads to blindness. After a number of years a high proportion of these patients develop frank tuberculosis of the lungs. A clinical diagnosis is often possible, but biopsy of a lymph node or skin lesion will give confirmation. The disease is unaffected by treatment.

THE PROLIFERATIVE GROUP (RETICULOSIS)

Hodgkin's disease is the most common member of this group. It is primarily a local disorder, in most cases first manifest as enlargement of lymph nodes in the neck, less frequently in the axilla, and rarely in the groins. In the majority of patients who present with enlarged cervical or axillary lymph nodes, skiagrams show a mediastinal mass. The process gradually becomes generalized with fever, anæmia, cachexia, and often stubborn pruritus. The local swellings disappear after irradiation but it is doubtful if life is ever prolonged by such treatment; few patients survive more than two-and-a-half years. There is perhaps hope of cure for those in whom the disease is confined to one superficial group of lymph nodes, amenable to complete surgical extirpation. Biopsy is the only method of assured diagnosis.

In *lymphoid leukæmia*, enlargement of lymph nodes frequently brings the patient under observation. This is commonly generalized from the onset and associated with spleno-hepatomegaly. Lymphocytosis of the peripheral blood confirms the diagnosis; but in many cases of the indolent type the total leucocytes are not increased, although the lymphocytes commonly exceed 3,500 per c.mm. In a proportion there is no lymphocytosis and, unless sternal puncture shows lymphoid transformation of the bone marrow, the diagnosis can only be made by biopsy. Symptoms may be few; the course is often prolonged and, particularly in the aged, may exceed ten years. Radiotherapy does not prolong life and appears at times to hasten the tempo of the disease; it should never be prescribed in acute cases, and in the chronic is best withheld until enlarged lymph nodes cause pressure symptoms or grave disfigurement. The place of urethane in treatment is as yet undefined.

In the less common types of reticulosis, the diagnosis can only be established by biopsy; two of these require mention. *Lymphoid follicular reticulosis* may appear as a local or systematized disorder; the course is prolonged, and radiotherapy, although at first symptomatically successful, frequently appears to hasten the malignant change which is a common termination. *Histiocytic medullary reticulosis* can often be diagnosed clinically: it is an acute or subacute affection with enlargement of the spleen and lymph nodes, fever, and profound leucopenia. Remission has followed splenectomy in one or two cases; irradiation is contraindicated.

THE NEOPLASTIC GROUP (RETICULOSARCOMA)

The reticulosarcomas are of several cytological types but their clinical behaviour is similar, irrespective of the histological picture. The most common is the *lymphoblastic reticulosarcoma*, which usually gives rise to a general enlargement of lymph nodes and splenomegaly; in the later stages the peripheral blood may contain an excess of lymphoid cells. The less differentiated forms appear more frequently as local tumours: sometimes in a superficial group of lymph nodes, sometimes within the thoracic or abdominal cavity, and occasionally in bone as the Ewing tumour. Multiple myelomatosis falls into this group. In all cases an initial response to radiotherapy is followed after an interval by systematization and the course of the disease seldom exceeds eighteen months. Precise diagnosis is impossible without biopsy. A certain proportion of reticulosarcomas arise in lymph nodes which have previously undergone a non-malignant enlargement: the instance of lymphoid follicular reticulosis has already been cited.

Metastatic carcinoma of lymph nodes is frequently the first sign of an occult primary tumour, particularly of those arising in the bronchi and upper respiratory tract. Biopsy is often required for diagnosis.

RONALD BODLEY SCOTT, D.M., F.R.C.P.

MIGRAINE

THE cause of this malady is still unknown. It has been ascribed to vascular dilatation in the brain and local œdema: it has been described as an allergic disorder, or dependent upon a variety of forms of peripheral irritation, such as eyestrain, gastro-intestinal upsets, and the like. There is no doubt that in some cases hepatic ineffi-ciency and gall-bladder disease seem to bear some relation to the malady. Endocrines have been inculpated, but the very definite menstrual headaches, which are also familial in character, do not belong to this group. The paroxysmal headaches and hypertensive crises of certain suprarenal tumours are also a separate entity. Menstrual headaches cease at the menopause, whereas, in migraine, although it may become milder in type after this age, the headaches certainly continue. At the moment some form of vascular disturbance holds the field, many of the above suggested causes being merely irritating or exciting factors of the paroxysmal head-ache; this is supported by the fact that if you ask a patient what precipitates an attack some will say emotion, worry, fatigue, others some irregularity of the bowels, a fatty meal, alcohol in the middle of the day, a stuffy atmosphere, a visit to the pictures, and so on, but nearly all will admit that much more often there is no apparent exciting factor.

Migraine occurs mainly in the more highly strung, intelligent and over-active individuals. It often begins in childhood, when it may be overlooked or diagnosed as bilious vomiting, sick headaches, cyclical vomiting or, in one or two cases which I have seen, when it has been associated with epileptiform convulsions, as epilepsy.

It is perhaps more common for migraine to arise in early adolescence and a few cases appear to begin in later life, but these latter should always be suspect, and carefully examined for more serious intracranial causes of headaches. Some of the cases appearing in middle life will on inquiry be found to be simple recurrences of migraine in adolescence. It is familial in its character and not infrequently associated in the same family with other disorders of neuropathic origin, such as epilepsy and asthma.

Migraine tends to decrease in severity after middle life, not infrequently the headaches disappear and ocular and sensory manifestations may alone represent the attack.

SYMPTOMS

The symptoms of this disorder are very varied. In the classical forms of severe or moderate severity, there are three definite stages. The attack may begin on wakening in the morning, or may arise at any time of the day. Some people appear to have prodromal discomforts by which they know an attack is pending, but more com-monly the attack begins with some feeling of giddiness, nausea, and visual dis-turbance. The *visual disturbances* or *aura* are of many types: an almost complete blindness, described by the patient as a thick mist, or a hemianopia, in which the patient says he sees half of everything. In other cases the patient describes flickering lights or spots, or a play of colours, or the well-known fortification figure. Hallucinations of vision have been described.

After a period of ten to thirty minutes the *headache* begins and steadily increases in intensity. It is a deep stabbing or boring pain, spreading from the frontal or temporal region over the head. *Nausea*, if present at the inception, persists, or actual vomiting may occur and be a marked feature of the attack. More often vomiting appears to terminate the paroxysm.

The pain, which may be agonizing, is increased by movement, noise or light. The patient lies with his head buried in the pillow, face ashen, utterly prostrated and incapable of any physical or mental effort. Occasionally *vasomotor disturbance*

is shown by flushing of one side of the face and pulsation of the temporal artery. There is in some instances a superficial feeling of coldness.

After a varying period of some hours the attack may pass off leaving the patient tired and shaken. At this stage a profuse *diuresis* may occur. More often sleep ensues, the patient waking free of headache and well again until another paroxysm occurs. In very severe cases the attack may last for days, in others it may cease and a dull persistent headache is left which continues until the next paroxysm.

Occasionally *aphasia* and even word blindness may precede or accompany the headache, and in a little girl of ten under my care the attacks were associated with a complete but temporary hemiplegia lasting a few hours.

Some sufferers from this malady describe *sensory symptoms,* such as paresthesiæ. These sensory phenomena are as a rule on the side opposite to the headache and not infrequently occur apart from the headache or alternate with it.

Ophthalmoplegia, partial or complete, has been described as occurring in very severe attacks of migraine, and may last for days or weeks. Cerebral syphilis or aneurysm of the carotid artery may give rise to a similar syndrome and should be excluded in cases of this character. Fortunately, not all cases of migraine are of this character, and in far the greater number the disorder is represented by mild recurring headaches with or without visual disturbances. These, although interfering with work and causing difficulty in reading and writing, do not completely incapacitate the patient from following his duties, or can be relieved if medication is given at the onset of the attack.

Attacks may recur frequently or at long intervals, increase in frequency being often associated with domestic anxieties, business worries, and other psychological factors.

DIAGNOSIS

Diagnosis should not be difficult when a patient presents with a history of recurring headaches of many years' standing, dating from childhood or adolescence, and more particularly when they begin on wakening, are unilateral, or are associated with visual disturbances and nausea.

Some of the rarer sensory and motor manifestations may give rise to apprehension of organic nervous disease, particularly when they occur alone. But the sensory phenomena of migraine cannot be mistaken for epilepsy as they are slow in production and leisurely in passing off and there is no loss of consciousness. Mistakes can, however, arise, and no case of apparent migraine, particularly when beginning in later life, should be dismissed without a careful examination of the central nervous system. Slowly growing intracranial tumours and repeated mild attacks of subarachnoid hæmorrhage may all present in the first instance with symptoms suggestive of migraine.

The patient's habits, diet, and methods of life should be fully investigated; all systems should be examined from this point of view, and of peripheral irritation or toxic foci. Occipital and supra-orbital neuralgias, sinus disease and other lesions of skull and cranial nerves, hypertensive headaches, chronic nephritis and other causes of periodic headaches, can all be eliminated by a routine examination.

TREATMENT

Treatment can be divided into treatment of the actual attack and treatment of the intervening period. Remedies for both, as in all cases of uncertain pathology, are numerous.

Treatment of the attack.—Mild cases often find relief in resting immediately an attack seems imminent and in taking one of the simple combinations of aspirin,

phenacetin and caffeine, or aspirin, phenacetin and codeine; one or two tablets will often suffice.

In the more severe attacks, rest is compelled by the character of the illness and should be carried out in a darkened room away from noise. Evaporating lotions or an ice-bag to the head may help the headache, or when there is a sense of chill a hot-water bottle to the feet. The simple analgesic remedies mentioned may be tried but will often fail, and vomiting, when it occurs early in the attack, precludes the use of drugs by mouth. Ergotamine tartrate is dramatically successful in some cases, but time has shown that it also may fail to give any relief. The drug can be given by mouth in tablets of 1 mgm. or in solution as a hypodermic injection in doses of 0.25 to 0.5 mgm. Two tablets may be taken at the beginning of an attack and repeated in two hours if necessary; they act best if allowed to dissolve under the tongue. They are disappointing in their effect in severe cases and the best result is obtained by injection: an initial dose of 0.25 mgm. should be given subcutaneously and repeated in one hour if no toxic effects, e.g. nausea, giddiness, are produced. It should not be used continuously, nor in pregnancy, nor in the middle-aged with arteriosclerosis. It is conveniently put up in tablets and ampoules under the trade name of "femergin".

When this drug fails, attempts may be made to procure sleep by any of the recognized hypnotics—opiates should never be given if they can possibly be avoided. The risk of habit is considerable; if used, the nature of this injection should never be disclosed.

Treatment during the intervening period aims at prevention, but is little more satisfactory than treatment of the attack. Phenobarbitone, $\frac{1}{4}$ to $\frac{1}{2}$ grain (16 to 32 mgm.), night and morning, or in conjunction with sodium bromide, 7 grains (0.45 gm.) thrice daily, helps to moderate the nervous element. The following mixture still has its advocates and is successful in some cases; it should be given for a prolonged period in dosage of 1 ounce (28.4 c.cm.) thrice daily.

R

Sodium bromide	..	10 grains (0.65 gm.)
Solution of trinitrate	..	1 minim (0.06 c.cm.)
Solution of strychnine	..	4 minims (0.24 c.cm.)
Dilute hydrobromic acid	..	10 minims (0.6 c.cm.)
Tincture of gelsemium	..	10 minims (0.6 c.cm.)

Many sufferers from migraine have their own cures, or learn to avoid certain actions or dietetic indiscretions which they know will induce an attack. A small dose of calomel once a week, morning salts, the liberal drinking of water, avoidance of fats, extra glucose with meals, all have their advocates and are simple and harmless expedients. Steps should be taken to improve the general health of the patient. Errors of refraction, septic foci, or gall-stones, may be initiating factors inciting to an attack. But their correction or removal, although sometimes beneficial, cannot be relied upon to prevent the attacks. Habits and diet should be considered and modified when necessary. Overwork, domestic and business worries are a frequent cause of exacerbations or worsening of symptoms. In severe cases, or when attacks are constantly recurring or permanent headache is present, a period of rest in bed with separation from all types of mental worry is often imperative and beneficial. This should be followed by a complete change of scene and a peaceful holiday.

Allergy.—When there appears to be sensitivity to certain articles of food, they may be eliminated from the diet, but skin reactions and desensitization on an allergic basis are not called for—attempts to relieve migraine on these lines have not proved very successful.

Surgical methods have been advocated and carried out on the cervical sympathetic, but they are not recommended.

E. BELLINGHAM SMITH, M.D., F.R.C.P.

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

The Onset of Syphilitic Aortitis

QUERY.—An Army officer who was a patient of mine died in 1944, and I am trying to get the authorities to admit liability to the widow. According to his history sheet, he stated that in 1916 he contracted, and was treated for, syphilis. There were no symptoms until 1944, when signs of aortitis developed. Wassermann reactions at that time were negative. The two questions to which I should like an answer are—Could heart symptoms be delayed from 1916 until 1944? Could the strain and stress of duties, involving being bombed, bring on valvular disease of the heart?

REPLY.—The clinical manifestations of syphilitic aortitis do not usually appear until ten to twenty years after the primary infection. Therefore, in the case in question, aortitis was most probably syphilitic. Trauma can cause rupture or injury of the valves, especially the aortic, but the diagnosis of traumatic valvular disease would require circumstantial evidence of the time of occurrence and nature of the trauma in relation to the onset of clinical signs of valvular disease.

D. EVAN BEDFORD, M.D., F.R.C.P.

The Treatment of Leucoderma in Syphilitics

QUERY (from a subscriber in Calcutta).—I shall be extremely grateful if you can advise me of any treatment for leucoderma. The Wassermann and Kahn reactions of the blood are both positive. At present I propose starting antisyphilitic treatment and penicillin.

REPLY.—Dr. H. McCormack, writing in the *Dictionary of Practical Medicine*, edited by another dermatologist, Sir Malcolm Morris, in 1921, p. 188, wrote that "the treatment of this condition is most unsatisfactory because, although it is possible to cause pigment to form in the de-pigmented areas, as by X-ray irradiation, such measures increase the pigmentation in the surrounding zone. The application of suitable cosmetics is the only satisfactory means of disguising the unsightly appearance". I entirely concur, and the position is unchanged to-day. It is necessary to be sure that the leucoderma is not secondary to the syphilis indicated in the question. If it be, the colour will return to normal about eight to twelve months after an antisyphilitic course of treatment, this has particular reference to leucoderma colli. Other depigmentations such as lepra and achromias

that have followed surface infections, are separate clinical problems, the latter re-pigment speedily. As a syphilitic may also have true vitiligo, antisyphilitic remedies will not necessarily cure the patient. The time-sequence of sore and eruption, if any, can indicate if the loss of pigment is syphilitic or not. Walnut juice, 1 in 1000 solution of Bismarck brown and 1 in 2000 solution of permanganate of potash, repeatedly applied, will achieve a good camouflage on exposed leucodermic areas.

W. J. O'DONOVAN, O.B.E., M.D., M.R.C.P.

Impotence Following Captivity in a Prison Camp

QUERY.—I have a male patient, aged forty-three years who has been happily married for about fourteen years and has one daughter aged eleven years. From 1942 to 1945 he was a prisoner in Japanese hands, when he lost 3 stone in weight and had an attack of epididymo-orchitis on the left side. Before being taken prisoner his marital sexual life was normal. Since returning to England he has gained 3 stone in weight, his physical condition is good and he feels well and full of energy. The left testicle is slightly enlarged, the epididymis and cord are somewhat thickened and sensation is somewhat diminished. The right testicle, epididymis and cord all appear to be normal. The husband and wife both wish to have another child, but the husband is unable to obtain a satisfactory erection and ejaculates only a minute amount of semen. Should I advise him to wait a year to readjust himself physically and mentally to civilian and married life? Is hormone therapy likely to be of any help?

REPLY.—Many cases of impotence have occurred amongst those returning from long internment in prison camps and it is probable that both physical and psychogenic factors are responsible for this. The poor diet and fatigue associated with imprisonment generally lead to the complete disappearance of sexual desire and of sexual manifestations, and this in turn arouses in the patient the fear that he has been made permanently impotent. In this case an attack of epididymo-orchitis has probably added to the patient's anxiety. It is therefore psychogenic factors that are now more likely to be responsible for his failure to recover his potency. He should first be assured that this lesion cannot possibly have any permanent effect on his sexual capacity and that with the

full recovery of his general health this will undoubtedly return. Injections of testosterone may be helpful if for no other reason than that they will have a strong suggestive action. Should potency not return as a result of them and of reassurance, the patient should be sent to a capable psychotherapist.

KENNETH WALKER, F.R.C.S.

The Treatment of Chronic Cardiac Oedema

QUERY.—I have a male patient, aged seventy years, who is suffering from chronic pancarditis with œdema. During the last eight years he has had mersalyl (2 c.cm.) intramuscularly, but these injections are now failing to produce diuresis. There is no albuminuria or hæmaturia. I should be grateful if you could inform me if it is usual for the effects of mersalyl to wear off after a period of years, and if so are there any other diuretics that could be used?

REPLY (from a cardiologist).—It is unusual for the effect of mersalyl to wear off, even after it has been used over a period of years. Without more information concerning the type of heart failure and the dosage of mersalyl that has been used, it is impossible to say whether or not this failure to produce diuresis is permanent. Should this be the case, however, it would be worth while using theophylline-ethylenediamine, which is sold under the trade names of cardophylin and aminophylline, and can be given either orally or parenterally. For continued use, the oral preparation should be used in dosages of $1\frac{1}{2}$ grains (0.1 gm.), three or four times a day. If a satisfactory diuresis is not obtained with this treatment, then the drug may be given intravenously or intramuscularly, in doses of 0.24 gm., twice weekly.

Potassium Chloride in Myasthenia Gravis

QUERY.—A patient suffering from myasthenia gravis has responded remarkably well to potassium chloride. What is the action of the salt? What is the dosage, and are there any toxic effects if it is taken in large doses over a long period?

REPLY.—The use of potassium chloride in the treatment of myasthenia gravis was introduced by Laurent and Walther in 1935 (*Lancet*, i, 1434). The theoretical basis of the treatment is that the effect of acetylcholine is "potentiated" by the potassium ion: there is no deficiency of potassium in the serum, although Cumings (*Brain*, 1939, **62**, 153) has shown that there is an abnormally high potassium content in the muscles in this condition. The dosage recommended by Laurent and Walther is about 4 to 6 gm., six times daily. Subsequent reports have not always been as enthusiastic as that of the original workers. The principal symptom produced by these large doses is a marked diuresis, but diarrhœa and nausea may also occur. Careful biochemical and clinical control is required if large doses are persisted in for a long period, and the drug is dangerous if there is any suspicion of renal abnormality.

E. N. ALLOTT, B.M., F.R.C.P.

PRACTICAL NOTES

Pulmonary Tuberculosis and Pregnancy

ATTENTION is drawn by A. L. Jacobs (*Journal of Obstetrics and Gynæcology of the British Empire*, August 1946, **53**, 368), to the conflicting views that are held concerning the incidence of tuberculosis in pregnant women, and the effect of the pregnancy upon the tuberculous lesion. As a contribution towards a solution of the problem he records the findings in an investigation at Paddington Hospital where, since 1943, a screen examination of the chest has been part of the routine examination of all women attending the antenatal department. During this period 4,430 women have been examined. Among these there were 68 (1.53 per cent.) who were found to have pulmonary tuberculosis. Further analysis showed that of these 68 women, 27 had active tuberculosis requiring immediate admission to hospital, 11 had a lesion described as "possibly active", whilst 30 were considered "probably inactive". As nearly 60,000 births occur annually in the County of London, and approximately ten times this number in England and Wales, it is clear that the routine introduction of mass miniature radiography in antenatal clinics will provide a problem of considerable magnitude, even if considered only from the point of view of hospital accommodation. Jacobs suggests that the solution of the problem lies in the use of the large general hospitals, to which patients would be admitted as soon as the tuberculous lesion was discovered. In such hospitals skilled medical and obstetric staff would be available, so that both the pulmonary and the obstetric condition could be dealt with simultaneously and satisfactorily.

The Treatment of Rheumatic Fever

As part of a symposium on rheumatic diseases, E. F. Rosenberg and P. S. Hench (*Medical Clinics of North America*, May 1946, **30**, 489) contribute a review of recent advances in the treatment of rheumatic fever. The following are among their conclusions:—Sulphonamide prophylaxis is recommended for individuals who have had rheumatic fever, and for this purpose sulphadiazine is probably the drug of choice, given in doses of 0.5 to 1 gm. daily. Dietary supplements of certain foods and vitamins may assist in maintaining general good health, but there is as yet no definite evidence of their value in preventing an initial or recurring attack of rheumatic fever. In institutions the control of air-borne streptococcal infections by means such as oiling of beds and floors, aerosols, and ultra-violet irradiation, are useful adjuncts in the prevention of rheumatic fever. There is no good evidence that the intravenous administration of salicylates has any advantage over oral administration, except in patients in whom gastro-intestinal intolerance prevents oral or rectal administration. In therapeutic doses, given orally, the hæmorrhagic effect of salicylates is of little clinical importance. Penicillin is ineffective in the treatment of acute rheumatic fever, but it is recommended for the control of streptococcal complications of the disease. Although rest is essential in the treatment of rheumatic fever, this restriction of activity should not be carried too far. A United States War Department memorandum is quoted with approbation:—"Even in a large proportion of individuals with residual cardiac lesions of rheumatic origin, moderate physical exercise is beneficial rather than harmful. Whether or not crippling heart disease results from rheumatic fever as a rule depends on whether repeated attacks occur."

A Trocar and Cannula for Intravenous Fluid Administration

A TROCAR and cannula designed for the easy administration of fluids by the intravenous route is described by R. V. Pratt (*Medical Journal of Australia*, May 4, 1946, **33**, 629). Constructed of stainless steel, with a well-fitting trocar within a cannula of 17 British Whitworth gauge internal diameter, the instrument is fitted with a rubber tubing adapter with a simple locking device for attachment to the fluid reservoir. The cannula has an effective length of 1.5 inches, and the distal end is made practically flush with the point of the trocar in order to minimize any resistance to the tissues penetrated. The trocar has a sharp point, similar to that of a triangular cutting-edged

needle with a long bevel. Above the butt-plate there is a substantial finger-grip, and this is all that needs to be held during the piercing of a vein. The advantages claimed for the new instrument are (1) the need for cutting down on a vein, as with the use of a blunt cannula, is obviated, and also the difficulties associated with inserting a needle attached to a reservoir of fluid under pressure into a vein; (2) the instrument can be left *in situ* in a vein without fear of its being too easily dislodged or of the accidental piercing of a vein wall by restless movements of a patient; (3) removal of the trocar quickly shows by the presence or not of blood if the cannula is within the vein; the adapter is then instantly locked and the infusion under way; (4) the cannula can as a rule be safely pushed along the lumen of a vein up to its full length of 1½ inches and is then held in place by a strip of adhesive plaster placed over the side arms; (5) should the flow stop, the adapter is quickly slipped off and the cannula cleared by
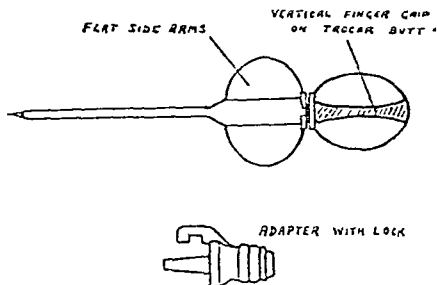
one motion of the trocar. The author states that he has used the instrument with the most satisfactory results for the continuous administration of pentothal and for drip infusions.

Dicumarol (Dicoumarin) in the Treatment of Coronary Thrombosis

DICUMAROL (3,3'methylene-bis-[4-hydroxy-coumarin]), which goes under the name of dicoumarin in this country, is an anticoagulant which has proved effective in the prevention and treatment of thrombophlebitis and embolism. I. S. Wright (*American Heart Journal*, July 1946, **32**, 20) records the use of the drug in the treatment of seventy-six patients with acute or recurrent coronary thrombosis, forty of whom had recurrent multiple thrombi in different areas of the coronary tree or had had repeated embolic phenomena, either pulmonary or in other areas, and thirty-three patients with uncomplicated first or second attacks of coronary thrombosis. Previous to administering the first dose of dicoumarin, the prothrombin

time is determined: the normal reading should be 13 to 17 seconds. If the prothrombin time is normal or lower, 300 mgm. dicoumarin is given orally in one dose. In the reported series the prothrombin time was determined each morning before the dosage of dicoumarin was decided. The drug was given in doses of 300 mgm. daily until the prothrombin time was 30 seconds, and in doses of 100 or 200 mgm. when the prothrombin time was between 30 and 35 seconds. When the prothrombin time reached 35 seconds, the drug was discontinued until there was a drop to below 30 seconds, when it was again introduced cautiously in doses of 100 to 200 mgm. Should hæmorrhagic manifestations occur, they can be checked by one or two transfusions of whole fresh blood (300 to 500 c.cm. each), or by the administration of vitamin K, or both. In most of the recorded cases dicumarol was continued for thirty days after the last thrombosis or embolism, the objective being to keep the prothrombin time between 30 and 50 seconds, particularly during the first two to three weeks; the dosage is then decreased slowly in order to allow the time to drop to 25 to 30 seconds, and then gradually to return to normal. In the recurrent group there was no evidence of additional thrombi or emboli after institution of the treatment: normally, this group would have had a very high mortality rate of about 60 or 70 per cent.; the death rate with dicumarol therapy was only 25 per cent. In the group of uncomplicated cases the mortality rate was only 12 per cent., compared with an anticipated death rate of 20 to 30 per cent. In eight cases in which post-mortem examination was carried out no evidence of hæmorrhage or other effects of dicumarol sufficient to produce death were found. Although the results are encouraging, it is stated that further investigation with larger groups of cases is necessary before the value of the routine use of dicoumarin can be definitely determined.

Intramuscular Calcification due to Injections of Calcium Gluconate

A CASE of intramuscular calcification due to the injection of calcium gluconate is recorded by J. W. McLaren (*British Journal of Radiology*, August 1946, 19, 314). Two days after birth an infant suffering from tetany was given an intramuscular injection into the buttocks of 10 c.cm. of a 10 per cent. solution of calcium gluconate. A further injection of 5 c.cm. was given on the 4th and 5th days after birth, and again on the 12th day. Three weeks later the buttocks became hard and tense, and a radiograph revealed the presence of extensive calcification in both buttocks and extending downwards to within a short distance of the knee joint. The calcification was still demonstrable three weeks later, but had disappeared at four months. The infant died of a congenital lesion of the heart at the age of four-and-a-half months, and autopsy showed that in the glutei the muscle tissue had been replaced by fibro-fatty tissue. Sections of these areas showed recent necrosis, chronic inflammation, fibrosis and small foci of calcification. Reference is also made to a case in which calcification occurred in the buttocks following the intramuscular injection of calcium penicillin (17 doses, each of 7500 units, at four-hourly intervals) in an infant a few days after birth. The factors responsible for this deposition of calcium are not known.

Testosterone Propionate in the Treatment of Advanced Mammary Cancer

ELEVEN cases of advanced cancer of the breast have been treated with large doses of testosterone propionate at the Breast Clinic of the Memorial Hospital, New York City, and the results are recorded by F. E. Adair and J. B. Herrmann (*Annals of Surgery*, June 1946, 123, 1023). Four of the eleven patients treated, one with soft tissue and three with osseous metastases, showed remarkable response to treatment. The total doses employed in the four cases were 3,975 mgm., 2,400 mgm., 4,100 mgm., and 2,150 mgm., respectively. The patient with soft tissue metastases, consisting of a hard nodular mass completely replacing the right breast, numerous skin nodules, nodules in the axilla and a hard nodular mass in the right subclavicular space, received 300 mgm. in the form of pellets implanted subcutaneously and 2,600 mgm. intramuscularly in doses of 200 mgm. over a period of nineteen days, followed by 25 mgm. three times weekly for eleven weeks. Examined thirteen days before cessation of treatment, the lymph nodes and skin nodules had completely disappeared and also areas of impending ulceration; no masses were palpable in the breast. X-rays of the chest, lumbar spine and pelvis were negative for evidence of metastatic disease. In the patient who received a total dose of 2,150 mgm., X-ray examination before treatment showed a large area of metastatic destruction in the left ala of the sacrum; a further X-ray examination after treatment showed progressive regeneration of the bone in the area of destruction and the patient was entirely free from pain. No toxic reactions were noted in the treated cases, although in three cases facial hirsutism developed. Although the

number of cases treated is stated to be too small to gauge the frequency of favourable reaction to testosterone propionate, the authors believe that, given in large doses, it may exert a favourable influence on certain cases of advanced carcinoma of the breast.

D.D.T. in the Treatment of Pediculosis Capitis

DURING the past eighteen months over 400 patients with pediculosis capitis have been treated with D.D.T. at a Nottingham clinic, and the results are recorded by A. D. Frazer (*British Medical Journal*, August 24, 1946, ii, 263). The formula employed was D.D.T. 2 per cent., naphtha 15 per cent., emulsifying agent 5 per cent., and water 78 per cent. The emulsion is thoroughly worked into the hair and scalp with a 2-inch (5 cm.) paint-brush. The patient is then free to go home and is instructed to wash the hair before attending the following day. At this second visit the nits are removed with a nit-comb. Usually one combing is sufficient, but with heavily infested heads two or more may be necessary. At the beginning of the series observation was maintained for three weeks before the patient was discharged as cured, but as the cure rate was 100 per cent. this procedure was later relaxed and, as it was found that the lice were killed in about half an hour after application of the emulsion, the hair was washed one hour after treatment and the combing carried out forthwith. In cases in which secondary infection was present the pediculi were attacked first by the above treatment, and on the second day when no live lice were present the hair was cut and the septic areas attended to. No signs of intolerance were observed, except in one case in which there was extensive impetigo in addition to the pediculosis, and in which inflammation and swelling of the nose, forehead and eyelids was present on the day after treatment but disappeared within a few days.

Pyramidon and Salicylic Acid

EXPERIMENTS carried out on animals by M. Danielopolu, M. Popesco and D. Crivetz (*Presse Médicale*, July 27, 1946, 54, 497) to determine the influence of pyramidon (amidopyrine), salicylic acid and sodium salicylate on the vegetative factors acetycholine, adrenaline, histamine, the Ca and K ions, and cholinesterase, showed that all three drugs exerted an inhibitory action on acetycholine, histamine and cholinesterase, but had no influence on the actions of the Ca and K ions. Pyramidon showed the strongest inhibitory action, and both this drug and salicylic acid were stronger than sodium salicylate in their action on cholinesterase. Histamine plays an important part in the etiology of neuralgias and migraine, and excellent results are stated to have been obtained in migrainous subjects by the administration for ten days of each month of 6 gm. sodium salicylate with 12 gm. sodium bicarbonate daily; pyramidon is reserved for the cure of the attack. Anaphylactic shock is also due to the liberation into the system of large quantities of histamine and acetylcholine, combined with decreased immunity to antigens, and pyramidon in conjunction with atropine is indicated for therapy, and also in asthma, in which the broncho-constriction is caused by the liberation of acetylcholine and histamine. In the treatment of acute polyarticular rheumatism or Bouillaud's disease, however, the drug of choice is salicylic acid, which, in addition to possessing a microbicidal action, inhibits the action of sympathin and leaves the myocardium under the influence of acetylcholine and thereby decreases the work of the heart. Pyramidon, on the other hand, by inhibiting the action of acetylcholine, augments the work of the heart and may aggravate the myocardial lesion. This action largely explains the occurrence of tachycardia and palpitations with pyramidon. Stress is laid on the necessity for prolonged rest in bed for cases of acute polyarticular rheumatism, and particularly in children, in whom the virus may cause considerable enlargement of the heart.

Trichomonas Infections of the Urinary Tract in Women

ACCORDING to B. Williams (*British Journal of Urology*, June 1946, 18. 63), "it is probable that *Trichomonas vaginalis* is the most frequent and important cause of urinary infection in the young female". An analysis of fourteen such cases showed that six were under the age of twenty, and the oldest was twenty-seven. Six of the patients were married. The symptoms consisted of urgency and frequency, scalding or burning pain on micturition, and a sensation after micturition that the bladder had been incompletely emptied. In five cases there was evidence of a spread of the infection to the upper urinary tract, whilst in several there were signs of salpingitis and pelvic peritonitis. In every case there was evidence of trichomonas infection of the vagina. The urinary symptoms usually subsided rapidly with rest, ample fluids and alkalis. Sulphanilamide or sulphithiazole was given in a few cases. Local vaginal treatment was given, but bladder lavage was not used. It is recommended that routine search for the organism should be made in all cases of

time is determined: the normal reading should be 13 to 17 seconds. If the prothrombin time is normal or lower, 300 mgm. dicoumarin is given orally in one dose. In the reported series the prothrombin time was determined each morning before the dosage of dicoumarin was decided. The drug was given in doses of 300 mgm. daily until the prothrombin time was 30 seconds, and in doses of 100 or 200 mgm. when the prothrombin time was between 30 and 35 seconds. When the prothrombin time reached 35 seconds, the drug was discontinued until there was a drop to below 30 seconds, when it was again introduced cautiously in doses of 100 to 200 mgm. Should hæmorrhagic manifestations occur, they can be checked by one or two transfusions of whole fresh blood (300 to 500 c.cm. each), or by the administration of vitamin K, or both. In most of the recorded cases dicumarol was continued for thirty days after the last thrombosis or embolism, the objective being to keep the prothrombin time between 30 and 50 seconds, particularly during the first two to three weeks; the dosage is then decreased slowly in order to allow the time to drop to 25 to 30 seconds, and then gradually to return to normal. In the recurrent group there was no evidence of additional thrombi or emboli after institution of the treatment: normally, this group would have had a very high mortality rate of about 60 or 70 per cent.; the death rate with dicumarol therapy was only 25 per cent. In the group of uncomplicated cases the mortality rate was only 12 per cent., compared with an anticipated death rate of 20 to 30 per cent. In eight cases in which postmortem examination was carried out no evidence of hæmorrhage or other effects of dicumarol sufficient to produce death were found. Although the results are encouraging, it is stated that further investigation with larger groups of cases is necessary before the value of the routine use of dicoumarin can be definitely determined.

Intramuscular Calcification due to Injections of Calcium Gluconate

A CASE of intramuscular calcification due to the injection of calcium gluconate is recorded by J. W. McLaren (British Journal of Radiology, August 1946, 19, 314). Two days after birth an infant suffering from tetany was given an intramuscular injection into the buttocks of 10 c.cm. of a 10 per cent. solution of calcium gluconate. A further injection of 5 c.cm. was given on the 4th and 5th days after birth, and again on the 12th day. Three weeks later the buttocks became hard and tense, and a radiograph revealed the presence of extensive calcification in both buttocks and extending downwards to within a short distance of the knee joint. The calcification was still demonstrable three weeks later, but had disappeared at four months. The infant died of a congenital lesion of the heart at the age of four-and-a-half months, and autopsy showed that in the glutei the muscle tissue had been replaced by fibrofatty tissue. Sections of these areas showed recent necrosis, chronic inflammation, fibrosis and small foci of calcification. Reference is also made to a case in which calcification occurred in the buttocks following the intramuscular injection of calcium penicillin (17 doses, each of 7500 units, at four-hourly intervals) in an infant a few days after birth. The factors responsible for this deposition of calcium are not known.

Testosterone Propionate in the Treatment of Advanced Mammary Cancer

ELEVEN cases of advanced cancer of the breast have been treated with large doses of testosterone propionate at the Breast Clinic of the Memorial Hospital, New York City, and the results are recorded by F. E. Adair and J. B. Herrmann (Annals of Surgery, June 1946, 123, 1023). Four of the eleven patients treated, one with soft tissue and three with osseous metastases, showed remarkable response to treatment. The total doses employed in the four cases were 3,975 mgm., 2,400 mgm., 4,100 mgm., and 2,150 mgm., respectively. The patient with soft tissue metastases, consisting of a hard nodular mass completely replacing the right breast, numerous skin nodules, nodules in the axilla and a hard nodular mass in the right subclavicular space, received 300 mgm. in the form of pellets implanted subcutaneously and 2,600 mgm. intramuscularly in doses of 200 mgm. over a period of nineteen days, followed by 25 mgm. three times weekly for eleven weeks. Examined thirteen days before cessation of treatment, the lymph nodes and skin nodules had completely disappeared and also areas of impending ulceration; no masses were palpable in the breast. X-rays of the chest, lumbar spine and pelvis were negative for evidence of metastatic disease. In the patient who received a total dose of 2,150 mgm., X-ray examination before treatment showed a large area of metastatic destruction in the left ala of the sacrum; a further X-ray examination after treatment showed progressive regeneration of the bone in the area of destruction and the patient was entirely free from pain. No toxic reactions were noted in the treated cases, although in three cases facial hirsutism developed. Although the

REVIEWS OF BOOKS

Introduction to Clinical Neurology. By GORDON HOLMES, C.M.G., C.B.E., M.D., F.R.C.P., F.R.S. Edinburgh: E. & S. Livingstone, Ltd., 1946. Pp. vii and 183. Figures 37. Price 12s. 6d.

IT is a well-established University practice for the introductory course of lectures in a subject to be given by the Professor, thus giving recognition to the fact that the clear presentation of the general principles upon which the understanding of a complex subject depends, is a task requiring the highest order of ability and experience. The English-speaking medical public has long been in need of such an authoritative statement of the essentials of clinical neurology and no-one was more fitted to supply that need than Dr. Gordon Holmes. In this book of one hundred and eighty pages he has set out clearly the essential scientific basis upon which the understanding of the normal and abnormal function of the nervous system is built up. Much of the book is an excellent presentation of the traditional teaching of the Queen Square School of Neurology and will remind those who were fortunate enough to attend them, of the author's teaching rounds and out-patient sessions. Other portions, notably the sections on cerebellar disturbances, sensation, vision and bladder function are largely built from the author's own original contributions to his subject, and the discriminating reader, in spite of the absence of references, will be reminded how large that contribution has been during the past thirty years. As an introduction to neurology this book should be read by all students of medicine, but as a masterly presentation of the scientific approach to clinical subjects it will be re-read by many who are no longer beginners. It is sure of a place among the classics of medical literature.

Patients and Appendicitis By SIR CRISP ENGLISH, K.C.M.G., F.R.C.S. London: J. & A. Churchill Ltd., 1946. Pp. vii and 155. Figures 4. Price 10s. 6d.

THE distinguished author of this book has set down the fruits of a long experience, in which the treatment of appendicitis has played a considerable part. The book is essentially a practical one, giving sound advice on the handling of the patient as well as on the treatment of the disease in its different phases. Sir Crisp English's main theme is the importance of early operation, to attain which end, not only must the practitioner be trained in the art of clinical examination and in the habit of decision, but

hospital, anæsthetist and ambulance services must be organized with a view to reducing the interval between the decision to operate and the operation itself. The pathology, clinical examination, diagnosis, and the indications for operation at different stages are fully discussed, and details, not alone of operative technique, but of the preparatory and after-treatment, are given in subsequent chapters. A full bibliography is appended. One of the most useful as well as one of the most characteristic chapters is the first, on " patients," in which the author discusses the important influence of the sympathetic handling of a family emergency on all its members, and of the special approach to fathers, mothers, sons, daughters, sick children and the aged. The author's outlook is summarized in his quotation from Warbasse: "the peculiarity of surgery is that the surgeon himself is part of the treatment".

The Anatomy of the Bronchial Tree. By R. C. BROCK, M.S., F.R.C.S. Oxford University Press, 1946. Pp. 96. Figures 142. Price 42s.

THE science and art of medical practice are forever expanding and developing so that most medical books require constant revision to bring them up to date. In the more restricted sphere of anatomy this is not so noticeably the case, and this excellent monograph, the result of many years of painstaking study, is likely to remain an authoritative work on the subject of the anatomy of the bronchial tree for all time. Each pulmonary lobe is carefully analysed according to its bronchial pattern, and running parallel with a clear anatomical discourse is an account of the clinical significance of this pattern in relation to the incidence of pulmonary abscess and its treatment. The studies are based on the evidence derived from skiagrams, post-mortem dissections, metal casts of the bronchial tree and clinical observations; and the whole is beautifully produced and copiously illustrated with effective colour drawings and charts. The chapters comprising the book were originally published separately in the *Guy's Hospital Reports*, of which Mr. Brock is himself the editor, and very occasionally it is possible to detect the absence of independent editorial comment or that of a sufficiently candid friend. Thus the sentence, "This is not so, and indeed the 5th or the 4th ribs are the most commonly correct ones" is the sort of solecism that even the most polished writers, such as the author, are liable to perpetrate in the small hours of the morning. One

urinary infection in women, especially when the infection occurs in the young, or during pregnancy or shortly after marriage. Failure to diagnose the presence of a vaginal infection with the *Trichomonas vaginalis* is common, and is usually due to inadequate search or to the fact that wet specimens are not taken and examined immediately. As a rule, the urinary infection subsides with the adequate treatment of the vaginal infection, but occasionally sulphonamides may need to be used.

Sulphathiazole Acid Jelly for the Treatment of Vaginitis and Cervicitis

A SULPHATHIAZOLE acid jelly with a new base (polyethylene glycol), which is stated to be non-irritating, non-staining and of agreeable odour, has been used in a series of cases of vaginitis and cervicitis by S. L. Siegler (*American Journal of Obstetrics and Gynecology*, July 1946, **52**, 1). The formula is:—

Sulphathiazole	..	..	..	10 per cent.
Lactic acid	..	..	..	3 per cent.
Acetic acid	..	..	..	1 per cent.
Sodium tetradecyl sulphate		..	0.1 per cent.
Polyethylene glycol ..	..	..	85.9 per cent.

A comparative study was made of the results obtained with (1) the acid jelly base alone; (2) the acid base with 1 per cent. iodine; (3) the acid base with 1 per cent. gentian violet; (4) beta lactose and sulphathiazole tablets. Applications of jellies or tablets were made once or twice daily, one application being made before retiring at night. Douches were not permitted. In the cases of cervicitis which were treated electro-surgically, applications were made postoperatively and in a few cases during waiting necessitated by the proximity of the menses. Of 230 cases of vaginitis treated, 83 per cent. were considered cured. Four cases of gonorrhœal vaginitis were given adjuvant oral sulphathiazole. In twenty-four cases of trichomonas treated with the polyethylene glycol acid jelly, good results were obtained in 75 per cent. Twenty-eight cases of monilia responded just as well to gentian violet polyethylene glycol acid jelly as to sulphathiazole jelly. Good results were obtained in six cases of trichomonas treated with 1 per cent. iodine in acid jelly base. Tablets of beta lactose and sulphathiazole were used in ten cases of trichomonas resulting in a cure rate of 80 per cent. In 152 cases of cervicitis treated with sulphathiazole-polyethylene glycol acid jelly alone or in conjunction with electro-surgery there was absence of profuse discharge, good control of bleeding, reduction in vaginal pH, and a marked reduction

in healing time, healing being complete in 90 per cent. of cases.

Vitamin E in the Treatment of Purpura

IN a brief note in *Science* (June 28, 1946, **103**, 762) F. Skelton *et al.* report successful results from the use of synthetic α-tocopherol acetate (vitamin E) in purpura. The dosage was 200-400 mgm. given by mouth, daily, and the antipurpuric effect appeared in seven to fourteen days, "but it seems that the treatment must be continued for long periods of time, if not permanently". Five patients with thrombocytopenic purpura, one of whom had failed to respond to splenectomy, responded well to this treatment, platelet counts and capillary fragility being quickly restored to normal. In one man with terminal purpura and aplastic anæmia associated with advanced lymphosarcoma there was great clinical improvement, as there was also in three women with menorrhagia and metrorrhagia, who bruised easily.

The Treatment of the Common Cold

ON the basis of the method of treatment of the common cold advocated some years ago by V. S. Cheney, which consisted in giving 60 grain (4 gm.) doses of sodium bicarbonate every two hours for three days to procure abortion of an oncoming cold, R. J. Stratton (*Pharmaceutical Journal*, June 22, 1946, **156**, 401) suggests the following regime:—One tablespoonful of a mixture of potassium citrate, 30 grains (2 gm.) and chloroform water, half strength, to ½ fluid ounce (24.2 c.cm.), to be taken two-hourly during the day until the cold is checked. In order to prevent a cold it is imperative to start the treatment *immediately* the first symptoms, such as sneezing or a tickling at the back of the throat, appear. The author of the original treatment recommended light diet and plentiful fluids (a large glass of hot water with each dose of sodium bicarbonate); hot fruit drinks are suggested as a pleasant substitute, and failing fresh citrus fruit the S.D.I. concentrated fruit cordials can be used. Another simple method of treatment for the oncoming cold is recorded by B. O. C. Pribram (*Lancet*, August 24, 1946, ii, 290): this consists in gargling two-hourly with a solution of 20 to 25 drops of dilute solution of ammonia *B.P.* in half a tumbler of water. The treatment should be begun as soon as the first signs of a cold are apparent.

THE ANGLO-SWISS MEDICAL CONFERENCE

A Conference between Swiss and British medical men, representing all branches of medicine and the related sciences, was held in Basle from September 16 to 21.

The Conference was initiated by the Swiss Academy of Medical Sciences, and the arrangements in England, which included the assembling of a group of speakers to give an account of contemporary British medical progress, were in the hands of an organizing committee representing the Royal Society of Medicine, the Royal Colleges, the Physiological Society, the Pathological Society, the Medical Research Council and the British Council. The Conference was attended by about 150 British visitors and an equal number of Swiss. The addresses, too, were about equally divided between the Swiss and the British representatives, and dealt with much of the work done in the two countries during the war years. The papers were, with only one or two exceptions, delivered in English, which the majority of Swiss scientists speak fluently, but half the seats in the auditorium were wired for earphones through which a running translation into German could be picked up.

In addition to the scientific proceedings a number of banquets had been arranged, and one day was set aside for a visit in the morning to the chemical works of Basle, and to the Rhine Falls and the Roman Amphitheatre at Augst in the afternoon. An example of the care which went to make the Conference successful was the publication at the beginning of the week of a special edition of the *Schweizerische Medizinische Wochenschrift*, containing the material to be discussed at the Conference, which was presented to all those who were attending the congress. It was appropriate that this Conference, the first post-war international meeting to include all branches of medical science, should have been held in the peaceful atmosphere of Switzerland.

Switzerland has had her present frontiers and name since 1803, but this was not her beginning but a recognition by the world of a Federation of Free City States that had inhabited the same mountains and pursued the same ideals since the beginning of history; that had kept alight the torch of freedom throughout the centuries and had held it high when it was extinguished in other lands; that had refused to be any man's servant and desired to be no man's master.

Swiss neutrality is rooted in her racial stock, which is a blend of the three main stems of the European family—Latins, Franks, and Teutons—and in her geographical position of the crossways of Europe. This neutrality is enduring and not temporary; spiritual and not political; determined and not opportunist. It has maintained the Red Cross, which would otherwise have had no meaning, and has preserved it as a force for good in times of evil.

Switzerland has avoided conflict, not timidly but courageously, and in doing so has benefited the world more than she could have done by the participation of her armies on one or other side. She has preserved humanity in a world grown callous. She has held her religious faith when cynicism and opportunism are rife. She has maintained political freedom when country after country has introduced sectional rule in the name of democracy; she has kept sanity and honoured reason when the herd instinct passes for public opinion and independent judgement is condemned as disloyal to one or other faction.

The people of Britain have always been bound to the Swiss nation by the link of common ideals, and attracted to their country by the unrivalled beauty of its scenery. But those who go to Switzerland in the summer to climb and swim or in the winter to ski, seldom know more of Basle than as a halting place for breakfast on the train journey, or as the source of the drugs that relieve their pains and cure their diseases. The visitors to the Conference were therefore delighted at the opportunity it gave them to see at leisure the beauties of this ancient and historic town standing at the head of the navigable Rhine, to study its treasures of art and architecture and to learn of the part it has played in European history. The University, which was founded about the same time as those of Oxford and Cambridge, which trained Erasmus and Holbein, which received numerous students from England during the 16th and 17th centuries, is now housed in magnificent modern buildings that formed an admirable setting for the Conference. Equally impressive was the Bürgerspital, just completed; a striking example of modern hospital architecture.

It is hoped that this Conference, at which medical instruction and enjoyment were so happily blended, will be followed by a return visit of Swiss scientists to Britain, and by similar meetings in other countries.

W. H. O.

slight criticism might be offered for consideration in further editions, and that is the order of the chapters. Chapter II deals with bronchial embolism and posture in relation to lung abscess. That it is placed so early in the book illustrates the author's approach to the subject, which is essentially practical and derives from clinical rather than strictly anatomical interest. To place this chapter here, however, involves the use of terms and concepts amplified in later chapters and, to a reader not already sufficiently familiar with the anatomy of the part, it reads, for once, somewhat inconsequentially. Such details, however, cannot detract from the superlative qualities of this work which is in the very best traditions of British medical literature. It should find its way on to the shelves of all who are interested in diseases of the chest; it would be difficult to conceive a doctor whose specialty was so restricted that he could afford to ignore the valuable material which is here so masterfully presented.

Gynæcological Endocrinology: For the Practitioner. By P. M. F. BISHOP, D.M. Edinburgh: E. & S. Livingstone, Ltd., 1946. Pp. viii and 124. Illustrated. Price 7s. 6d.

THE practitioner has long been bombarded by literature from chemical firms on the subject of sex hormone therapy in the female. He has been confused by the volume of material sent to him, the multiplicity of names used for similar products, and by the changing indications for their use. Dr. Bishop has come along and in a pocket-sized book has sorted out many of his troubles for him. Most practitioners will be grateful to him. He has put forth the current clinical practice with accuracy and has indicated also the main outlines of the theory underlying the use of the sex hormones. In these days, when it seems almost impossible for women not to receive indiscriminate endocrine treatment, perhaps a stronger word of warning might have been given, but in general the balance has been well held.

NEW EDITIONS

IN the preparation of the sixth edition of *Antenatal and Postnatal Care*, by FRANCIS J. BROWNE, M.D., D.SC., F.R.C.S.ED., F.R.C.O.G. (J. & A. Churchill Ltd., 25s.) complete revision has been carried out, although it is only two years since the appearance of the previous edition. Among new material added are sections on penicillin in the treatment of syphilitic women during pregnancy and its use in sulphonamide-resistant gonorrhœa; the influence of rubella and other infective diseases on con-

genital abnormalities; angular pregnancy; acroparæsthesia; and new information on the Rh factor and erythroblastosis, placenta prævia and the toxæmias of pregnancy.

Milk: Production and Control, by W. CLUNIE HARVEY, M.D., D.P.H., M.R.San.I., and HARRY HILL, F.R.San.I., A.M.I.S.E., F.S.I.A., in its second edition (H. K. Lewis & Co. Ltd., 37s. 6d.) represents, as stated by the authors, the position of the milk industry as it now stands after the difficult war-time period. Despite the many drawbacks due to war-time economy and restrictions, the industry has progressed, and the new edition of this work, which presents the industry in all its aspects, provides a wealth of interesting and instructive information.

THE addition of some new illustrations to *An Atlas of the Commoner Skin Diseases*, by HENRY C. G. SEMON, D.M., F.R.C.P., in its third edition (John Wright & Sons Ltd., 50s.), all beautifully reproduced by direct colour photography from the living subject, adds greatly to the value of this remarkable aid to diagnosis. The plates so vividly reproduce the different skin affections presented that with the aid of the author's notes diagnostic difficulties are reduced to a minimum. The author and his collaborators are to be congratulated on their achievement, and the publishers on the production.

A Handbook of Radiography, by JOHN A. ROSS, M.R.C.S., L.R.C.P., D.M.R.E., in its second edition (H. K. Lewis & Co. Ltd., 10s. 6d.) has been brought up to date in all sections. The work, which is intended mainly for students and radiographers, opens with a chapter on the care of the patient, and after discussion of technical details proceeds to instructions for taking radiographs of the different parts of the human body and then to the techniques of the various forms of radiological examination. The final chapter deals with elementary X-ray physics.

IN the second edition of *The Principles of Anatomy*, by A. A. ABBIE, M.D., D.SC., PH.D. (Angus and Robertson Ltd., 12s. 6d.) the author stresses the importance of genetics and their influence upon human development. Although the work has been entirely rewritten the author's original purpose has been maintained, that is, to assist students to realize the close relationship of biology in their study of human anatomy. The new edition is well illustrated, and a useful glossary of the terms employed is included.

The review of *A Short Practice of Surgery*, by Hamilton Bailey and McNeill Love in the July issue (p. 79) was of the 7th edition (not the 5th).

PNEUMONIA

By J. G. SCADDING, M.D., F.R.C.P.

*Physician and Senior Lecturer in Medicine, British Postgraduate Medical School;
Assistant Physician, Hospital for Consumption and Diseases of the Chest, Brompton.*

THE older nomenclature of the pneumonias was based almost exclusively upon anatomical features. This system of nomenclature remains current usage, but is clearly in many respects less satisfactory than one based upon the somewhat complete present-day knowledge of specific etiological agents. So long as only supportive treatment was available for pneumonia patients, an anatomical diagnosis was sufficient for most practical purposes. The development of specific serum therapy for pneumococcal pneumonias made it necessary to recognize one of the specific etiological groups, and this showed clearly that cases which under the morbid anatomical nomenclature might be called lobar pneumonia or broncho-pneumonia might belong to the same etiological group. The sulphonamides and penicillin, which have superseded the cumbrous method of serum therapy in pneumonia, are much less specific in their action and are effective against a wide range of infections; but their introduction has, if anything, increased the necessity for a re-classification of the pneumonias upon an etiological basis. If these powerful agents are to be used, there should be a reasonable assurance that the infecting agent is susceptible to their action.

CLASSIFICATION OF ACUTE PNEUMONIAS

Although classification on an etiological basis is possible for a large number of pneumonias which are due primarily to the action of a virulent organism upon a susceptible host, there remains a considerable group of pneumonias in which the inception of the disease is mainly due to non-specific adverse factors acting on the respiratory tract, often of a more or less mechanical nature. These consist chiefly of factors reducing the efficiency of the defences of the lower respiratory tract against invasion by infected secretions from above, and correspond roughly with the secondary broncho-pneumonias and hypostatic pneumonias of the older classification; they are essentially infected atelectases, in which the mechanical factors leading to the development of atelectasis may be regarded as the chief *cause* of the pneumonia, enabling organisms not normally invasive to set up inflammatory processes. For lack of a better term I use that of "aspiration" pneumonias to describe this group; using aspiration to mean not only gross inhalation of material from outside the respiratory tract but also the aspiration into the finer divisions of the broncho-pulmonary tree of endogenous secretions.

NOTES AND PREPARATIONS

NEW PREPARATIONS

DERMUCID [6 per cent. albucid (sulphacetamide) in a vanishing cream base] has been prepared for the treatment of septic affections of the skin, impetigo, folliculitis barbæ and similar conditions. It is stated to be easily applied and readily absorbed by the dermis. The manufacturers are British Schering Ltd., 167-169 Great Portland Street, London, W.1, who issue the cream in jars of 12.5, 25 and 50 gm., containing 6 per cent. albucid. Literature can be obtained on application.

SOLUBLE THIOPENTONE—BOOTS—Soluble thiopentone is the British Pharmaceutical name for an intravenous anæsthetic consisting of a mixture of 100 parts by weight of the mono-sodium derivative of 5-ethyl-5-(1-methylbutyl)-thiobarbituric acid, and 6 parts by weight of exsiccated sodium carbonate. The advantages claimed for this anæsthetic are ease of administration and portability, non-inflammability, and the quiet respiration produced thereby. It is supplied in boxes of 6 and 25 ampoules of 0.5 gm., with ampoules of sterile distilled water of 10.5 c.cm., price 10s. 7½d. and 39s. 1½d., respectively, and in boxes of 6 and 25 ampoules of 1 gm., with ampoules of sterile distilled water of 20.5 c.cm., price 14s. 5½d. and 53s. 7d. An explanatory booklet can be obtained from the manufacturers, Boots Pure Drug Co. Ltd., Station Street, Nottingham.

THE BRITISH RED CROSS SOCIETY

A Department of Welfare Service for distressed or disabled members of the civilian community, has been inaugurated under the auspices of the British Red Cross Society, with Dr. Harold Balme, Medical Officer in charge of Rehabilitation to the Ministry of Health, as Director. The Service will also provide after-care for crippled and invalid children and for the aged infirm. Air Marshal Sir Harold Whittingham, has been appointed Medical Adviser to the Society.

MEDICAL LITERATURE FOR EUROPE

THE Director of Health, European Regional Office, U.N.R.R.A., writes:—"Reports and requests from U.N.R.R.A. Missions in Europe make it abundantly clear that the greatest expressed need of doctors in the liberated countries is for medical literature covering the war years, so that they may bring themselves up to date with advances in unoccupied countries. I am therefore appealing for complete sets of general and specialist medical and nursing journals covering approximately the war years. They should be sent to Dr. H. Hadaway, Room 1934, Health Division, U.N.R.R.A., 19 Portland Place, London, W.1. (Tel.: Langham 3090/341), and carriage will be paid if requested. If it is felt that the sets cannot be given free of charge, a price should be stated before the sets are forwarded to us and we will try to obtain authority for their purchase."

TUBERCULOSIS NEWS

A Memorandum on B.C.G. (Calmette-Guérin Bacillus Vaccine), by PROFESSOR W. H. TYTLER, has been published by the Tuberculosis Association, Manson House, 26 Portland Place, London, W.1. The Memorandum gives an historical and scientific review of B.C.G. and a description of the methods of vaccination and dosage. There is also a useful bibliography. *Empire and Colonial Tuberculosis: A General Survey*, by PROFESSOR S. LYLE CUMMINS, published by the National Association for the Prevention of Tuberculosis, Tavistock House, Tavistock Square, London, W.C.1 (price 5s.), gives a description of the work of the National Association in different parts of the Empire. The splendid work that is being done by the Association is evident from the statistics: to take only one instance, in Trinidad, where tuberculosis was previously almost epidemic, the death rate of 275 per 100,000 in 1896-1900, in 1943 was only 100 per 100,000.

OFFICIAL PUBLICATION

On the State of the Public Health During Six Years of War, published by H.M. Stationery Office, price 5s., is a report by the Chief Medical Officer, Sir Wilson Jameson, on the activities and the results of the health services during the war years. The report, which covers all branches of the Health Services and also includes vital statistics and a chapter on future plans, is of outstanding interest.

susceptible subjects. The bacteria include the pneumococcus, hæmolytic streptococcus, Friedländer's bacillus, *Staph. aureus*, Pfeiffer's bacillus, tubercle bacillus, and other organisms listed in section 1 (A) of table I. There is abundant evidence that invasion of the lower respiratory tract of susceptible individuals by organisms of any of these groups is sufficient to cause a spreading inflammatory reaction in the lung, with exudation into the alveoli. Information about the virus pneumonias is much less complete, and in many instances when a virus is known to be capable of causing by itself an inflammatory reaction in the lung, it appears likely that in human disease it is most frequently accompanied by a bacterial agent in the lung lesions. This is the case with the viruses of influenza and of psittacosis, which have been the most completely investigated of the viruses associated with pneumonia in the human subject. Recently, routine radiological examinations have shown that localized penumonic consolidations pursuing a generally benign course are of frequent occurrence in certain outbreaks of epidemic respiratory infections. There is evidence that some of these outbreaks, to which it has become customary to apply the unfortunate and logically indefensible term "primary atypical pneumonia", may be caused by a pneumonotropic virus, but it is likely that a high proportion of the pneumonias which occur in these circumstances should be regarded as belonging to the "aspiration" group.

Aspiration pneumonias.—The importance of mechanical factors in the pathogenesis of pneumonia has been very differently assessed by different observers. The concept that many post-operative chest complications are essentially atelectases, often of lobar extent, in which bacterial infection of varying gravity may occur, was an important step in the understanding of these conditions, and led to a more fruitful approach to the problem of their prophylaxis and treatment. On the other hand, the contention of some observers, notably Coryllos, that pneumococcal pneumonia is essentially lobar atelectasis infected with pneumococci is not tenable; the previous work of Blake and Cecil on experimental pneumococcal pneumonia in monkeys has shown beyond doubt that typical pneumococcal lobar pneumonia is due to the specific invasive powers of pneumococci in the lungs of a susceptible animal, in which the organism causes an inflammation spreading in the interstitial tissue which may be likened to a cellulitis.

In many instances in which the defences of the bronchial tree against invasion from above are diminished, secretions collect in one or more bronchi or bronchioles; beyond the obstruction thus caused air is absorbed, giving rise to areas of atelectasis which become infected by any organisms which may be present in the aspirated secretions. In this way many post-operative, hypostatic and post-bronchitic pneumonias are produced. It has been demonstrated that iodized oil introduced into the nostrils of a sleeping person can be found the next morning in one or more broncho-pulmonary segments. This constitutes a mechanism by which it is possible for infected secretions from the upper respiratory tract in any condition of acute or chronic catarrh to be aspirated into a broncho-pulmonary segment

The pneumonias can be classified under two main headings:—(A) Acute specific pneumonias; (B) aspiration pneumonias.

TABLE I
CLASSIFICATION OF ACUTE PNEUMONIAS

(1) *ACUTE SPECIFIC PNEUMONIAS*

(A) BACTERIAL *Str. pneumoniæ* (pneumococcus)	Synonyms: lobar, croupous or fibrinous pneumonia, pleuro-pneumonia. Complete diagnosis includes anatomical distribution and pneumococcal type
Str. hæmolyticus Friedländer's bacillus *Staph. aureus* } *H. influenzæ* }	often in association with a virus, e.g. that of influenza
M. tuberculosis	Pneumonic pulmonary tuberculosis
B. anthracis	Wool-sorter's disease
P. pestis	Pneumonic plague
P. tularensis	Pneumonic form of tularæmia
E. typhi and *E. paratyphi* } *B. melitensis* and *B. abortus* }	In both typhoid and undulant fevers, although pneumonia due to the causative organism has been described, pneumonia when it occurs is nearly always due to other organisms
(B) VIRUS	
Influenza } Psittacosis }	Although experimentally these viruses have been shown to be capable of causing by themselves pneumonic lesions, the pneumonias associated with them in man are almost always associated also with independently pathogenic bacteria
Measles	Also associated with pathogenic bacteria
Other unidentified viruses	Some cases of "primary atypical pneumonia"
(C) RICKETTSIAL	In association with the typhus fevers
(D) PLASMODIAL	In *P. falciparum* malaria
(E) DISEASE OF DOUBTFUL ETIOLOGY	In which a specific pneumonia may occur
Rheumatic fever	Non-specific lung lesions, especially atelectasis, also occur

(2) *ASPIRATION PNEUMONIAS*

(A) DIFFUSE	Synonyms: secondary broncho-pneumonia, infected atelectasis
	Types: post-operative, post-bronchitic, hypostatic, deglutition, inhalation
(B) CIRCUMSCRIBED	"Benign circumscribed pneumonia" Synonyms: "pneumonitis", probably many cases of "primary atypical pneumonia"
(C) SUPPURATIVE	Synonyms: suppurative pneumonitis, necro-suppurative broncho-pneumonia, lung abscess

Acute specific pneumonias.—Many agents, both bacterial and virus, are known to be specifically invasive for the lungs and to cause pneumonias in

common bronchogenic type form a special type of localized aspiration pneumonia. The occurrence of lesions of this type presumably depends upon the presence of pyogenic and necrotizing organisms in the infected mucous plug. A short classification of the acute pneumonias based upon these considerations is given in table 1.

The frequency of the commoner types of pneumonia varies from time to time and from place to place. This is especially true of those pneumonias in which a virus plays a part in the etiology. Among the causes of acute specific bacterial pneumonias the pneumococcus is, of course, overwhelmingly the most frequent, followed by the hæmolytic streptococcus, *Staph. aureus* and Friedländer's bacillus. The frequencies with which these organisms and a mixed group of other organisms occurred in a large series reported by Bullowa and Gleich from New York between 1928 and 1935, and in a small series investigated at Hammersmith Hospital, London, in 1938-39, are shown in tables 2 and 3.

TREATMENT

The considerations outlined above have an important bearing upon the treatment of pneumonias; measures appropriate for aspiration pneumonias, for instance, being contraindicated in primary pneumococcal pneumonias. There are certain points to be borne in mind in relation to each group of pneumonias.

Acute specific bacterial pneumonias.—Many of these are sensitive to sulphonamides: pneumococcal and hæmolytic streptococcal cases almost invariably, and staphylococcal to a less extent and to a narrower range of drugs. Friedländer's bacillus is not sensitive to most of the sulphonamides, although there is some evidence that large doses of sulphadiazine may have some effect on infections by this organism. Penicillin is effective against the same organisms as sulphonamides in this group of pneumonias, and in addition has a much stronger and more reliable action on *Staph. aureus.* It has no effect on Friedländer's bacillus; the only agent known to be effective against this organism is streptomycin, work on which is still in the experimental stage and which is not yet available for clinical use.

In general, the chief point in treatment in this group is the use of an effective chemotherapeutic or antibiotic agent in those cases caused by sensitive organisms; such cases constitute a large majority of the group.

Pneumonias associated with virus infections.—Therapeutically this is a difficult group. No known agent is effective against virus diseases of the lung. In influenza, however, it is known that pneumonic changes, although to a partial and variable extent due to the virus, are almost invariably associated also with pathogenic bacteria, often belonging to groups known to be sensitive to sulphonamides or penicillin. It is therefore reasonable to employ these agents in cases of pneumonia associated with influenza, although as yet there is no statistical evidence of their effect. The less severe pneumonias presumed to be due to specifically pneumonotropic viruses, which form part

and there cause a single focus of pneumonia, the course of which will depend upon the nature of any organisms which may be present. Often these organisms are not themselves very invasive; the resulting pneumonic reaction then pursues a benign course and may not produce any distinctive symptoms to suggest its presence. This mechanism is undoubtedly responsible for a large number of the pneumonias which have been described under the title of "primary atypical pneumonia", or by earlier authors as "pneumonitis". In the aspiration pneumonias generally, the bacteria most frequently found in the sputum are *Str. viridans*, non-hæmolytic streptococci, pharyngeal neisseriæ, Pfeiffer's bacillus, and sometimes small numbers of the higher and less invasive types of pneumococcus; in fact, a bacterial flora similar to that of the upper respiratory tract in normal persons.

TABLE 2

INCIDENCE   OF   PNEUMOCOCCAL   AND   NON-PNEUMOCOCCAL PNEUMONIAS

(Bullowa and Gleich, New York 1928-35).

	Number	Percentage of total
Pneumococcus.. ..	3817	77.8 per cent.
Str. hæmolyticus ..	126	3.3 per cent.
Staphylococcus ..	59	1.2 per cent.
Friedländer's bacillus ..	36	0.7 per cent.
Others	869	17.0 per cent.

Pneumonias of mixed etiology.—It is clear that an "aspiration" pneumonia may develop into an acute specific pneumonia if an organism capable of causing a specific cellulitis in the lung is present in the aspirated secretions. Pneumonias presenting features of both the aspiration and the acute specific groups may thus arise. This is well illustrated by post-operative pneumonias in which, if the atelectatic element is overcome by suitable measures and there are no specifically invasive organisms in the secretions, rapid resolution may occur; but, on the other hand, the picture may change from that of "massive collapse" into that of a bacterial pneumonia if such organisms are present. The aspiration pneumonias form a very varied group, which

TABLE 3

ORGANISMS ASSOCIATED WITH APPARENTLY PRIMARY PNEUMONIAS OF LOBAR EXTENT

(Hammersmith Hospital 1938-39).

	Number	Percentage of total
Pneumococcus.. ..	59	67.8 per cent.
Str. hæmolyticus ..	4	4.6 per cent.
Staph. aureus	2	2.3 per cent.
Mixed organisms not including the above ..	22	25.3 per cent.

includes many cases showing a suppurative tendency. Lung abscesses of the

there has been a favourable response it may be cut down to 0.5 gm. four-hourly or 1 gm. three times a day. In cases which have responded favourably the total duration of treatment will be five or six days, giving a total dose of 25 to 30 gm. The usual precautions about fluid intake and alkalization of the urine should be observed while sulphonamides are being given; the latter is less important with sulphamezathine than with other sulphonamides.

In severe cases, or if vomiting makes oral administration uncertain, treatment should be started with the intravenous injection of the soluble sodium salt of the chosen sulphonamide. This is best given in a constant drip glucose saline infusion. The advantage of this method is that it ensures an adequate fluid intake and thus helps to avoid renal complications. An initial dose of 2 gm. of the sodium salt followed by further administration at the rate of 1 gm. four-hourly is appropriate. If, as is usually found, there is a favourable response within twelve or twenty-four hours, administration can be continued by the oral route. If there is a poor response to treatment, with no improvement in the patient's condition after forty-eight hours, the cause should first be sought. At this stage the bacteriological reports on the material obtained at the beginning of treatment should be available and may provide a clue to the failure to respond. It may be that an organism poorly sensitive or not sensitive to the sulphonamide in use, e.g. *Staph. aureus* or Friedländer's bacillus, is present. The possibility of acute tuberculous pneumonia or of the pneumonia being secondary to some underlying lesion of the lung should also be considered. If all these possibilities can be excluded, local complications, especially the early development of empyema, should be considered; if there is any suspicion of this, the chest should be needled over the area most dull to percussion. If none of these factors is present, and the organism is one sensitive both to sulphonamides and to penicillin, or is relatively insensitive to sulphonamides and sensitive to penicillin, such as *Staph. aureus*, penicillin treatment should be instituted.

PENICILLIN TREATMENT

Penicillin may be indicated not only in cases which have failed to respond to sulphonamides or which are caused by organisms resistant to sulphonamides, but also as primary treatment in certain instances. These include cases known to be due to a staphylococcal infection and cases in which sulphonamides are contraindicated; for instance, in patients known to be sensitive to sulphonamides or in whom there is antecedent renal disease. In addition, in patients who are severely ill at the time when treatment is begun, who are severely dehydrated or who have troublesome vomiting, it may be that penicillin is from the beginning a preferable form of treatment to sulphonamides, in spite of the greater difficulty of its administration. In some severe cases it may be advantageous to give sulphonamide and penicillin treatment simultaneously. Three-hourly intramuscular injection remains the most reliable method of giving penicillin, and in a serious case of pneumonia in which penicillin is indicated it is probably best to administer it by this

of the group which has been described as primary atypical pneumonia, have in general been found not to respond to either sulphonamides or penicillin.

"Aspiration" pneumonias.—This group includes a wide range of types, varying greatly in severity. The more severe pneumonias in this group are generally secondary to some grave antecedent illness. These are the hypostatic and terminal pneumonias, and in them prognosis is governed by the antecedent illness. Many of the post-operative pneumonias fall into this group. At the other end of the scale of severity there are the benign circumscribed pneumonias which may complicate any catarrhal condition of the respiratory tract, and which may produce only the mildest symptoms. In all these pneumonias the importance of "mechanical" factors must be borne in mind; from the therapeutic point of view, if they are diagnosed early in their course and the patient's general condition warrants it, an effort to secure re-expansion of atelectatic areas by encouraging cough and by attention to postural factors may secure unexpectedly early resolution. At the same time organisms suspectible to sulphonamides or penicillin are frequently present in these cases, and the administration of these agents, especially if indicated by a bacteriological examination, should not be omitted.

Practical considerations.—In the practical management of pneumonias much will depend upon the laboratory and other facilities available. In the case of apparently primary pneumonias of lobar extent the pneumococcus is so frequently the causative organism that in the absence of convenient laboratory facilities it is reasonable to treat all cases of this sort in the first instance as if they were caused by the pneumococcus. However, if laboratory facilities are available, material should be obtained for bacteriological examination before beginning treatment. Sputum, if a good specimen is available, is the best material and can generally be obtained by encouraging the patient to cough. If it is quite unobtainable a throat swab may give useful information but is less reliable. Lung puncture is justifiable only for special purposes. In any gravely ill patient a blood culture should also be carried out before treatment is begun.

SULPHONAMIDE TREATMENT

In a case of average severity, after a specimen of sputum has been obtained for culture, sulphonamide treatment should be instituted. There is now a wide range of sulphonamides effective against the pneumococcus, hæmolytic streptococcus and to a less extent *Staph. aureus*. Of these, three which are commonly available and which are relatively little liable to cause nausea and vomiting are sulphathiazole, sulphadiazine and sulphamezathine; the first two of these, having acetyl derivatives of low solubility, are more apt than the last to give rise to renal complications, and therefore in routine treatment sulphamezathine is probably preferable. Adequate dosage is essential: for an adult, an initial dose of 3 gm. followed by 1 gm. four-hourly, or in severe cases 1.5 gm. four-hourly, should be given. Dosage at this level should be continued for forty-eight or seventy-two hours, when if

INFLUENZA

By J. N. CRUICKSHANK, *M.C.*, D.Sc., M.D., F.R.C.P., F.R.F.P.S.

Physician, Glasgow Royal Infirmary.

THE term "influenza" is often used in a loose way to cover a group of febrile disorders of various kinds. Within recent years there has been a better appreciation of what constitutes influenza, and how it can be differentiated from febrile catarrh, "grippe" and similarly named epidemic disorders which have, in common with influenza, a stage of infection of the upper respiratory tract with catarrhal manifestations. Observations on the history of influenza will be found by those interested, in the work of Crookshank (1930), and also in the more recent review by Andrewes (1942).

ETIOLOGY

From the time of the discovery of the so-called influenza bacillus, *H. influenzæ*, by Pfeiffer in 1892, until the confirmation of the virus nature of the influenzal infection in the thirties of the present century, there were a good many rather ill-defined notions as to the mode of transmission of the disease. Attempts to treat and prevent influenza by means of vaccines prepared from various bacterial sources met with disappointing results. It is only since the study of viruses in relation to this and similar infections became properly established on experimental lines that a true estimate of the incidence, course and epidemiology of influenza has become possible. In this connexion, the researches of such workers as Stuart-Harris (1943), Laidlaw (1935) and Andrewes (1942) laid the foundations of the modern conception of the nature of this disease.

The earlier discoveries regarding the virus nature of the influenzal infection seemed to indicate a much simpler state of affairs than is now believed to exist. For one thing, it has become clear that there is not a single virus, but a group of viruses, which can be related etiologically to the group of clinical syndromes included in the term "influenza", and that this virus group is, in its turn, related to certain epizoötic virus infections, for example, swine fever. It was, indeed, in connexion with this disease that Shope (1936) was first able to demonstrate the symbiotic relations between the virus agent and the bacterial agent in the production of the clinical syndrome, swine fever. He showed that in the pig the virus alone produced disease so mild that it could be detected only by careful observation, and that, in his experimental series at least, the bacillus alone seemed harmless. The experimental study of the virus factor in human influenza was made difficult by the specificity shown by the infection, and no real progress was made until the work of Smith *et al.* (1933, 1935) on ferrets made possible the transmission of the infection to laboratory animals. Their conclusions from this work are expressed with such reserve that they may be quoted here as an example of

method, notwithstanding the inconvenience to nursing staff and patients of such frequent injections: 15,000 to 25,000 units three-hourly will maintain an effective concentration to deal with most of the penicillin-sensitive organisms causing pneumonia. Penicillin treatment should be continued for several days after defervescence, and in the average case of pneumonia this will mean treatment for five or six days. In a few cases of pneumonia caused by organisms usually sensitive to sulphonamides in which no response was obtained to sulphonamide treatment, I have given a short course of penicillin, 100,000 to 150,000 units, while continuing the sulphonamide, and have found that the therapeutic response produced by the penicillin was maintained by continued sulphonamide treatment.

The usual supportive treatment of pneumonias and the treatment of complications will not be discussed in this article. One point, however, should be mentioned; during the treatment of pneumonia by sulphonamides or penicillin a close watch must be kept for the development of effusions and empyemas. These may arise during treatment and give rise to no very distinctive symptoms, presenting later under the guise of "delayed resolution".

The treatment of aspiration pneumonias will clearly be dependent upon which of the many types of this group is under consideration. The mildest of all may require no special treatment of any sort. The principles of treatment in the group may be exemplified by the treatment of post-operative pneumonias. Here, as has already been indicated, there is a considerable mechanical factor, early attention to which may cause rapid alleviation of the condition before there has been any severe invasion by bacteria, although infection by specifically invasive organisms may occur at any stage. It is therefore wise in such cases to start as with apparently primary pneumonias by obtaining material for bacteriological examination and instituting standard sulphonamide therapy. At the same time the mechanical factors should receive careful attention. The patient must not be allowed to remain constantly in the unfavourable posture which he will naturally tend to adopt. He will most often be found lying in the position which prevents him from coughing, *i.e.*, the position in which the affected area of lung is least favourably placed for the expulsion of secretions. He should be made to change his position into a more favourable one and encouraged to cough. Voluntary deep breathing is helpful; administration of 7 per cent. carbon dioxide in oxygen may have a comparable effect in uncooperative patients. No tight bandages which might obstruct full respiratory movement should be permitted. Abdominal distention, if present, should receive attention. Only in special circumstances will more drastic measures, such as bronchoscopy or bronchial suction, be required. If these measures to deal with the mechanical factor result in rapid relief of symptoms and disappearance of physical and radiological signs, it is usually safe to discontinue the sulphonamide treatment. If, however, this happy result does not ensue it may be assumed that infection by an invasive organism has occurred and treatment similar to that suggested for apparently primary pneumonias is indicated.

approach has its limitations (Stansfeld and Stuart-Harris, 1943). The relations between the various types of virus are evidently fairly close, and this raises interesting speculations regarding the possible identity between the animal and human infections. Shope (1936), for example, concludes from a study of the incidence of neutralizing antibodies for swine influenza virus in the sera of human beings of different ages that the similarity between it and human influenza is very close. He even feels justified in concluding that the virus of swine fever was probably the surviving prototype of the agent primarily responsible for the great pandemic of influenza in 1918. This had also been suggested by Laidlaw (1935).

SYMPTOMATOLOGY

For descriptive purposes, certain clinical types of influenza are differentiated, but it is probable that these do not correspond to the different types of virus, or even to the different secondary or symbiotic bacterial infections associated with them. An outstanding feature of influenza is the variety of its clinical manifestations. There is, however, a certain tendency for groups of symptoms to predominate in individual waves of an epidemic. It is usual to refer to the following common clinical types of influenza:—

(1) Simple or febrile type.
(2) Pneumonic type.
(3) Abdominal type.

Simple febrile type.—In the simple febrile type of influenza, the onset of the attack is usually rapid. The commonest and almost constant prodromal symptom is headache, usually frontal. Associated with it there are vague but often quite severe pains at the back of the eyes, in the limbs and in the loins. These give the sensation of being "in the bones" rather than in the muscles or joints. The temperature rises sharply [102° to 104° F. (38.9° to 39.4° C.)], but there is seldom an actual rigor. The pulse rate and respiration rate become elevated, but only in proportion to the degree of fever. There is at this stage no disturbance of the pulse-respiration ratio unless some unusually early pulmonary complication is developing. During this initial febrile phase the usual general accompaniments of fever are noted—dry skin, dry mouth, furred tongue, malaise and anorexia. Epistaxis may occur. The blood pressure tends to fall 10 to 20 mm. Hg. The white cell count shows an early polymorphonuclear leucocytosis. In the absence of complications this is replaced by a leucopenia with a relative fall of granulocytes and rise of lymphocytes. After a period of twenty-four to thirty-six hours the symptoms tend to change. The degree of febrile reaction usually diminishes and with it the degree of general malaise; but the temperature tends to show irregular elevations, particularly in the afternoon or early evening, for five to seven days. At first there is little evidence of catarrh, the nasopharyngeal mucous membranes being rather dry, red and congested, but later there is nasal discharge and coughing brings up some tracheobronchial mucus or muco-pus. If there are no complications, the attack

moderation in the statement of deductions from scientific work of the kind:—

" We consider that the evidence given above strongly suggests that there is a virus element in epidemic influenza and we believe that the virus is of great importance in the etiology of the human disease. . . . Our results with ferrets, so far as they have gone, are consistent with the view that epidemic influenza in man is caused primarily by a virus. It is probable that in certain cases this infection facilitates the invasion of the body by visible bacteria, giving rise to various complications. . . . Decisive evidence on this point, and indeed on the importance of the virus we have described, can, we feel, only be secured by intensive study during an influenza epidemic, since direct experiments on man are fraught with difficulties."

Since then good progress has been made in the direction of establishing the truth of the conclusions suggested by these writers. It has been possible, using the ferret, to study the different types of virus infection associated with influenza in man, and to compare them with the effects of similar virus infections in animals, such as dog distemper and swine fever. For example, using a technique devised by Hirst *et al.* (1942), a study of influenza in Britain was made in 1942-43, by Stuart-Harris, Glover and Mills:—

Garglings from the pharynx of patients suffering from influenza, administered to ferrets and implanted in developing eggs during the epidemic early in 1942, failed to give any evidence that the mild influenza prevalent at that time was associated with either A or B type of influenza virus. Early in 1943, however, an increase in the number of respiratory infections was found to be associated with serological evidence of virus B infection, whilst later in the season (March to June) small scattered outbreaks of virus A infection were similarly identified. This is a good example of the way in which the type of infection can be determined in influenzal outbreaks. A basis can thus be secured for the study of the clinical differences in the types of virus infection.

Comparisons with epizoötic virus infections have shown points of interest in relation to the epidemiology of human influenza. There is still much to be worked out in this connexion and many of the details are controversial. Thus, in studying the epidemiology of swine influenza, it has been found that virus infection does not spread indiscriminately through a drove, or from drove to drove. It is probably widely seeded and dormant for some time before the disease breaks out: activated, it would appear, almost simultaneously throughout the animal population. For some months after such an outbreak, further cases are infrequent. Shope (1941) has found evidence in the earlier literature to suggest that human influenza may originate at many different points and spread secondarily from each of these separate foci. The rapidity of spread of the virus infection may thus appear to be greater than it really is, the widespread outbreak of the disease being due to a stimulus acting simultaneously over an area containing many masked foci of latent virus infection. In support of this idea it has been demonstrated that in some recorded pandemics of influenza the rate of spread of the disease has been much faster than human movement could carry it.

In spite of attempts to distinguish between virus types in man, it has so far been impossible to lay down criteria by which the differential diagnosis can be made on clinical grounds alone in the individual patient. The general predominance in an epidemic of one type or another of the virus can be determined by serological tests and animal inoculations, but even this

to be looked upon as exaggerated or without organic basis. The handling of the patient at this stage requires particular care, and no symptom should be dismissed as "functional" or "just due to nervous debility" until it is certain that some underlying organic cause is not being overlooked. It is therefore evident that the late stages of the disease, often referred to as "post-influenzal", may be more serious and more difficult to treat satisfactorily than the initial acute phase of the simple febrile type of influenza.

Pneumonic type.—The pneumonic type of influenza has been regarded in the past as something different from the simple febrile form, but there does not seem to be any reason for making it a separate entity. Even in the simple form of influenza there is a variable tendency to complications affecting the respiratory tract. There are, however, epidemics in which these respiratory infections play a much greater part than is usual, and in which the frequency of pneumonia, including broncho-pneumonia of a rapidly developing type and the slowly resolving pneumonitis, or atypical pneumonia, is so great, and its effects so serious, that they may well be referred to as outbreaks of the pneumonic type of influenza. In the epidemic of 1918 there was a high incidence of this type, with rapid progression from full health to extreme prostration and toxæmia, a widespread pneumonic consolidation of the lung parenchyma and a tendency to the formation of pus. When the patient did not immediately succumb, there was a high incidence of pulmonary abscess, gangrene of the lung and empyema. Many patients, however, developed an extreme cyanosis of a peculiar heliotrope tint, and died within twenty-four to forty-eight hours. Such cases had many points of resemblance to the pneumonic type of plague.

Abdominal type.—This type of influenza is popularly known as "gastric flu". It is often little different from a simple febrile attack, apart from a greater degree of nausea and anorexia than usual, but from time to time outbreaks occur in which acute gastro-intestinal symptoms predominate. During an influenza epidemic it is important to avoid the danger of overlooking outbreaks of bacillary dysentery in which the symptoms may be similar.

Infection with Pfeiffer's influenza bacillus (*H. influenzæ*), either in association with virus influenza or, less commonly, independently of it, may strike at any tissue, and so there may occur the so-called "influenzal lesions" of the central nervous system, of the upper respiratory tract and accessory sinuses, of the eyes, and even of the endocardium or pericardium. These are often serious in their nature and tend to have a high mortality rate.

TREATMENT

PREVENTIVE MEASURES.—Like other epidemic diseases that assume pandemic proportions from time to time, influenza seems to have some association with conditions likely to cause a general lowering of resistance. Outbreaks have at various times in the past been found to occur in relation to war or the aftermath of war, but there have been other serious outbreaks in

fades out from this stage, but is usually followed by a period of lassitude and mental depression which seem out of proportion to the severity of the initial illness. The duration of this "post-influenzal debility" which figures largely as a cause of industrial incapacity, is variable. So long as it lasts—and it may go on for weeks without apparent diminution—the patient is incapable of sustained mental or physical effort. In cases in which it is unduly prolonged there is a danger of quite serious psychological effects. A characteristic feature of this phase of depression and asthenia is that, suddenly, without any apparent reason, it disappears "like the raising of a curtain". This feature is so striking that it may be of diagnostic value in cases in which the nature of the illness has been in doubt. In other cases, the amount of catarrhal reaction in the upper and middle levels of the respiratory tract may be considerable, and convalescence in such patients may be delayed because of the persistence of tracheo-bronchitis, sinusitis or otitis media.

More serious respiratory complications of this simple febrile type of influenza include bronchiolitis and bronchitis, broncho-pneumonia and pneumonitis ("unresolved pneumonia") and its sequelæ. Pleurisy may occur, but is usually secondary to or an accompaniment of the more serious pulmonary complications, such as broncho-penumonia. When the upper respiratory tract bears the brunt of the catarrhal process there may be a series of complications which cause much distress to the patient and may even be a danger to life. Otitis media is fairly common, but there may also be extension to the mastoid region or to the internal ear. Acute mastoiditis is not uncommonly a sequel to a relatively mild initial attack of influenza. Involvement of the internal ear may cause prolonged nerve deafness or an alarming type of vertigo that may simulate the effects of a space-occupying intracranial lesion. Catarrhal inflammation, or even suppuration, in the antra, frontal and ethmoid sinuses may give rise to serious and prolonged disability. Ill to bear at the best of times, these forms of sinusitis are particularly apt to give rise to psychological disturbances in the patient who is already suffering from the toxic depression of the late stages of an influenzal attack. The teeth may become involved, either from the development of an actual pulpitis or from referred pain from the sinus inflammation, so that "neuralgia" is added to the patient's ordeal.

Inflammatory reactions occur also in the eyes, conjunctivitis, keratitis and iridocyclitis being the more common manifestations.

Neuritis, or at least pain referred to the course of certain peripheral nerves, is often a troublesome feature during the later stages of recovery. Like headache, neuralgia and other subjective symptoms associated with upper respiratory tract catarrh, these pains in the extremities may be difficult to assess. There is such a thing as true neuritis complicating influenza, but often the symptoms are present without there being evidence of this. Pain in muscles and joints may occur and give rise to similar diagnostic difficulties.

As many of these complications and sequelæ of influenza have few objective signs, the symptoms of which the patient complains so bitterly are apt

Persons exposed to influenzal infection are more liable to fall victims if they are over-tired or chilled, or are depressed or inadequately fed, but there is no evidence that any modification of the diet will afford a reliable method of lessening the incidence of infection.

Aerosols.—Air purification is an obvious way of lessening the risk of spreading infection during an influenza epidemic. Adequate ventilation, which is something different from a draught of cold damp air and should take into account control of temperature and humidity as well as the rate of exchange of air, is the most obvious means of atmospheric purification, but it may be difficult to control. For this reason the method of choice may have to be the addition of something to the air of the "inhabited closed space" in question which will diminish its bacterial and virus content. The use of aerosols has been developed in this connexion and it is now recognized to be one of the most effective ways of diminishing the spread of droplet infection in halls, theatres and other enclosed spaces. The work of Laidlaw and his colleagues (1943), has demonstrated the value of aerosols in controlling the spread of influenza. Various chemical substances and mixtures have been used in these aerosols, but there is, as yet, no final decision as to which is the most effective: solutions of hypochlorite, various phenol derivatives, propylene-glycol vapour, and so forth. Exposure of the air to ultra-violet light has also been used as a method of "sterilization".

The results from the use of aerosols have been sufficiently good to justify their compulsory use during epidemic periods as an alternative to complete closing of places of entertainment and similar premises, where the crowding together of individuals increases the risks of infection to a dangerous degree. Even at times when there is no actual epidemic, the use of aerosols is likely to be of benefit in reducing the incidence of the common cold and similar infections. The efficiency of aerosol sprays is maximum when their use is combined with proper control of atmospheric temperature and humidity.

PALLIATIVE TREATMENT.—Treatment of the individual patient during an attack of influenza is largely symptomatic. For the protection of others he should be isolated as soon as the onset of the disease is recognized, and his attendants should cover their mouths and nostrils with a handkerchief or a mask when within range of his droplet spray.

In addition to rest in bed and protection from disturbance, the patient should be given a sufficient amount of fluid to ensure that his renal output is well maintained. It is useful to add to this an alkali, such as potassium citrate in some palatable form. Diet should at first be restricted to fluids, such as glucose, fruit drinks, tea or the simpler milk foods. After the initial febrile period with its accompanying anorexia is past the patient may be allowed a full light diet. During the period of depression and asthenia he may need to be encouraged to take more than he feels inclined for. A simple alkaline bitter mixture may be useful at this stage. Attention to the regulation of the bowels and care of the mouth and skin are obvious parts

which no such general underlying factor can be shown to have been present. The periodicity so often seen in the epidemiological studies of disease is not so clean-cut in influenza as in some other infections. There is a rough trend towards an eleven-year cycle, with seasonal swings within this, which show a fair correspondence with certain climatic conditions involving a low atmospheric temperature and high humidity. It is probable, however, that the associated tendency to the crowding of individuals into imperfectly ventilated spaces, with increased opportunity for the spread of droplet infection, is the precipitating factor in the outbreaks. The main point in this connexion is the difficulty of predicting an epidemic outbreak with sufficient certainty to justify the use of preventive measures which have for the most part a short period of efficacy. Once an epidemic phase has been recognized, however, its course may be modified and its area of spread restricted by the application of certain measures.

Anti-virus vaccines.—In dealing with closed communities, such as schools, residential institutions and military units, it is possible to insist on care being taken to minimize the risk of droplet infection and to increase the resistance of the group by inoculation with a mixed virus vaccine. There is now evidence that this form of immunization does lessen the case incidence in population groups exposed to an epidemic outbreak of influenza. The protection is not complete and its duration is short, but the effect is sufficient to justify the use of prophylactic anti-virus vaccination in such circumstances. The modern form of concentrated vaccine of the Hirst type is prepared from the centrifugalized deposit from the allantoic fluid of chick embryos. Mixed cultures from both types of virus are used in equal parts and homogenized. These are given subcutaneously. It has been found that a single dose of 2 c.cm. of such a vaccine produces a sharp rise in the titre of the recipient's serum, lasting for six to nine weeks, with a further gradual fall up to the end of five months. A large series of observations by Hirst *et al.* (1942) and others showed that even with a relatively small dose of this vaccine (1 c.cm.) there was a sharp rise of two-and-a-half times the pre-inoculation level by the end of one to two weeks. The maximum protection appears to be during the second week after the injection of the vaccine. It has been estimated that in a closed population so protected the average attack rate can be reduced by about 85 per cent. during the second week. The protection begins to fall off after that, but even at the end of six weeks the attack rate may be only 40 per cent. of that expected. As the protection of vaccination becomes effective from about the eighth day it is probably well to wait until there is evidence that the epidemic wave is actually beginning before making the inoculations (*J. Amer. med. Ass.*, 1945). It should be added that not all observers support the claims made for the protective value of these vaccines, and that there have been series of cases recorded in which, for some reason or another, no appreciable degree of protection was found to have been given.

Persons exposed to influenzal infection are more liable to fall victims if they are over-tired or chilled, or are depressed or inadequately fed, but there is no evidence that any modification of the diet will afford a reliable method of lessening the incidence of infection.

Aerosols.—Air purification is an obvious way of lessening the risk of spreading infection during an influenza epidemic. Adequate ventilation, which is something different from a draught of cold damp air and should take into account control of temperature and humidity as well as the rate of exchange of air, is the most obvious means of atmospheric purification, but it may be difficult to control. For this reason the method of choice may have to be the addition of something to the air of the "inhabited closed space" in question which will diminish its bacterial and virus content. The use of aerosols has been developed in this connexion and it is now recognized to be one of the most effective ways of diminishing the spread of droplet infection in halls, theatres and other enclosed spaces. The work of Laidlaw and his colleagues (1943), has demonstrated the value of aerosols in controlling the spread of influenza. Various chemical substances and mixtures have been used in these aerosols, but there is, as yet, no final decision as to which is the most effective: solutions of hypochlorite, various phenol derivatives, propylene-glycol vapour, and so forth. Exposure of the air to ultra-violet light has also been used as a method of "sterilization".

The results from the use of aerosols have been sufficiently good to justify their compulsory use during epidemic periods as an alternative to complete closing of places of entertainment and similar premises, where the crowding together of individuals increases the risks of infection to a dangerous degree. Even at times when there is no actual epidemic, the use of aerosols is likely to be of benefit in reducing the incidence of the common cold and similar infections. The efficiency of aerosol sprays is maximum when their use is combined with proper control of atmospheric temperature and humidity.

PALLIATIVE TREATMENT.—Treatment of the individual patient during an attack of influenza is largely symptomatic. For the protection of others he should be isolated as soon as the onset of the disease is recognized, and his attendants should cover their mouths and nostrils with a handkerchief or a mask when within range of his droplet spray.

In addition to rest in bed and protection from disturbance, the patient should be given a sufficient amount of fluid to ensure that his renal output is well maintained. It is useful to add to this an alkali, such as potassium citrate in some palatable form. Diet should at first be restricted to fluids, such as glucose, fruit drinks, tea or the simpler milk foods. After the initial febrile period with its accompanying anorexia is past the patient may be allowed a full light diet. During the period of depression and asthenia he may need to be encouraged to take more than he feels inclined for. A simple alkaline bitter mixture may be useful at this stage. Attention to the regulation of the bowels and care of the mouth and skin are obvious parts

of the nursing routine, which may have to be supervised by the practitioner if no skilled nursing is available. For the relief of discomfort and the reduction of fever, aspirin (acetylsalicylic acid), alone or in conjunction with phenacetin and codeine, is a popular remedy. It is advisable to give some simple alkali along with it, and the old-fashioned diaphoretic mixtures, with ammonium acetate and sweet spirit of nitre, have much to be said for them. Patients who are upset by aspirin or are not relieved by it might be given instead phenacetin, 4 grains (0.25 gm.), combined with caffeine citrate, 1 grain (65 mgm.).

Chemotherapy.—There is a vogue for using small doses of sulphonamides, but it should be remembered that such drugs given prophylactically, when a chill is felt to be imminent, may simply cause the patient to become sulphonamide-resistant, so that if serious respiratory or other complications arise they will be of no avail. There is no evidence that sulphonamides have any effect on the influenza virus in ordinary therapeutic doses. Their only value in influenza is in the treatment of secondary bacterial infections. This applies also to such antibiotics as penicillin.

Post-febrile symptoms.—After the febrile phase of influenza, the asthenia, hypopiesis and depression which are so common may be found to respond to strychnine, 5 minims (0.3 c.c.m) of the liquor, three or four times a day, either alone or in combination with phosphates and iron, as in the compound syrups. For children and others who are intolerant of strychnine, a simple bitter mixture may replace it. The alkaline gentian mixture of the *B.P. Codex* is suitable for such patients. In a few cases there may be a degree of anæmia sufficient to make the use of an iron preparation desirable. The patient may ask if he should have vitamin tablets, and there is no reason for withholding these, even if there should be no evidence of gross vitamin deficiency. In a few cases there are indications for giving them in quite large doses, for example, when the patient's appetite remains impaired, or when there are signs of some degree of peripheral neuritis.

Finally, there is no doubt that in most cases a holiday, however short, is the most effective means of preventing a too protracted convalescence.

References

Andrewes, C. H. (1942): *Proc. roy. Soc. Med.*, **36**, 1.
Crookshank, F. G. (1930): "Epidemiological Essays", London.
Edward, D. ff., Ilford, W. J., and Laidlaw, P. P. (1943): *J. Hyg.*, **43**, 1.
Hirst, G. K., Rickard, E. R., and Whitman, L. (1942): *Proc. roy. Soc. Med.*, **50**, 129.
J. Amer. med. Ass., 1945, **127**, 222.
Laidlaw, P. P. *et al.* (1935): *Lancet*, i, 1118.
Shope, R. E. (1936): *J. exper. Med.*, **63**, 669.
—— (1941): *Ibid.*, **74**, 49.
Smith, J. W., Andrewes, C. H., and Laidlaw, P. P. (1933): *Lancet*, ii, 66.
—— —— —— (1935): *J. exper. Path.*, **16**, 291.
Stansfeld, J. M., and Stuart-Harris, C. H. (1943): *Lancet*, ii, 789.
Stuart-Harris, C. H., Glover, R. E., and Mills, K. C. (1943): *Ibid.*, ii, 790.

SORE THROATS AND TONSILLITIS

By T. B. LAYTON, D.S.O., M.S., F.R.C.S.

Surgeon, the Throat and Ear Department, Guy's Hospital.

THE phrase a "sore throat" sounds self-explanatory. It is anything but that. It is used for a subjective symptom, an hypothesis and a disease by doctors and by patients, and all at different times use it in different senses, and each, on each occasion, uses it differently.

STATIC SORE THROAT

As a symptom sore throat has two manifestations: there is a static soreness and a soreness of movement. The first may arise in two ways: from a diffuse but low inflammation over a considerable area, and from a muscular ache. The former occurs under conditions of bad hygiene, as among sailors living in a destroyer, or children in an overcrowded basement. It may also arise in persons leaning over individuals' mouths, until they become used to this, as in dental students starting to work on patients, or those working in a throat department after being away for a while. It may be limited or diffuse. It passes with the correction of the hygiene or in time.

The muscular ache may arise from excessive use of the voice or in rheumatic disease. The first is not often recognized since the aphonia overlays it. The second needs more study. The thought of the medical profession has for so long been concentrated upon the decision to remove tonsils on insufficient grounds that pharyngology as a subject has been neglected, and the subjective symptoms referred to this part of the body have not been critically analysed by present-day physicians. Such aches may account for the story told by some that all cases of acute rheumatism are ushered in by tonsillitis. Such symptoms are almost certainly one reason why tonsillectomy in rheumatism of middle age has given such poor results. Of these sore throats, those will be more common in winter in which the causal conditions are then more frequent; as when the family crowds into an already stuffy room and shuts the windows to retain more heat; and in those forms of rheumatic disease that are more frequent in the winter season.

SORE THROAT ON MOVEMENT.—Movement increases all these static sore throats, and in all inflammations of the mobile part of the upper respiratory tract soreness on swallowing occurs in varying degrees. But there is also a soreness of movement special to itself: this is the soreness due to a palate defective by nature or from trauma when it fails efficiently to swab the posterior pharyngeal wall on swallowing. The upper respiratory tract needs a balanced proportion between the cross-section of its airway and the surface area of its walls. When the airway is in excess, drying of the mucous membrane results. The main site of this disharmony is the nose; but a subsidiary area lies at the junction of the oro- and the naso-pharynx. The proportion is gauged by looking, while the tongue depressor is used in quiet respiration, at the posterior pharyngeal wall and noting how far in

front of this the soft palate hangs and the freedom with which it does so. When the pharynx is unduly deep or the soft palate is not free, this wiping is deficient and dryness of the posterior wall results. The degree of this is assessed by the want of reflection from its surface.

The unwiped pharynx.—When the dryness is marked, pain on swallowing results. The condition may be suspected by the history. It is present, or worse, on waking in the morning. A cup of tea relieves it. By midday it is slight or nonexistent. But it has another characteristic. Just as all static "sore throats" are present and even worse on swallowing so all those of movement, with this one exception, are there to a slight degree in the resting position. The patients will not have to go through the movements of swallowing to answer whether the throat is sore or not at the moment the question is put. In this one type of sore throat they may, or will have to do so: they shut the mouth, suck some saliva into the back of it and swallow before replying "Yes, it is." This form of sore throat depends more upon the dryness of the air than upon its temperature. It is therefore liable to be worse in summer and in winter when these are dry, rather than in those seasons that are usually wet. The condition becomes more distressing when there blows across the surface of the earth that cold wind that comes to us from the east.

THE HYPOTHESIS OF THE SEPTIC FOCUS

The phrase "sore throat" has played a great part in the "focus of sepsis" hypothesis, due to the difficulty of talking to patients about their illnesses. Amongst ourselves we invent words and phrases designed to indicate exactly the pathological conditions from which patients are . or may be suffering, and then these terms have to be interpreted to the patient in phraseology understood by laymen. They then use a phrase of ours for the disease of which it is but a symptom. Last stage of all we copy them, and come to think that every patient who tells us he suffers from "sore throats" has an enduring and harmful lesion. We confirm our suspicion by seeing a crescent of redness in the anterior pillars of the fauces, unmindful of the fact that this is an area of mucous membrane of constant mobility and has therefore a deeper colour than its surroundings, just as has the arytenoid region in the larynx. This aspect of the problem of "sore throats" bears no relation to the seasons; it varies rather with the conditioning of the mind of the doctor to the "focus of sepsis".

TONSILLITIS

And so we come to "tonsillitis". Surely, this is a simple enough anatomico-pathological term? Yes, but not so the problem underlying it. The tonsil is inflamed in any inflammation of the upper respiratory tract, and it may also be inflamed as a disease by itself. The former are diseases spread by droplet infection and in this country are winter disorders: scarlet fever and other types of hæmolytic streptococcal inflammation of the tract, the two virus diseases of influenza and measles with their secondary hæmolytic streptococcal affections. The tonsillitis that is a disease by itself, and arises from

the organisms residing in the tonsils alone, is not. This again, is strictly a manifestation of the hæmolytic streptococcus.

The triple syndrome.—This form of tonsillitis is characterized by its recurring nature, and by a triple syndrome:—First, there are general symptoms besides the pain on swallowing; secondly, this pain is very real; thirdly, the attack lays the patient low in such a way that he takes as many days to recover after rising from his bed as he has found it necessary to take to it. The old clinicians used to classify tonsillitis into "parenchymatous" and "follicular". The primary tonsillitis is usually follicular in distribution; but other organisms, including that of diphtheria, may produce the same; and an inflammation of the upper respiratory tract from droplet infection may take on a follicular distribution when it reaches the tonsils. On the other hand, the primary tonsillitis may be parenchymatous, although usually this distribution is, I think, the result of droplet infection. The course of the attacks and their recurrent nature, independent of the seasons, are more important in sorting out the primary tonsillitis from other forms of inflammation of the upper respiratory tract than the anatomical type of the inflamed tonsil. Therefore in this diagnosis interrogation is more important than inspection of the faucial areas.

THE BACTERIOLOGICAL EPIDEMIC

There is a bacteriological epidemic that precedes the clinical winter epidemic, with an increase of the flora in the nose and nasopharynx. Therefore the streptococcal inflammations spread by droplet infection at this time are grafted to a mucous membrane already damaged by other infections. But it is in the results of these infections as much as in their incidence that the winter complaints of the upper respiratory tract reside. In this country the rhino-pharyngological year may be divided into the "swelling-up" and the "swelling-down" periods, whether as a result of the subclinical bacteriological epidemic or merely of physical conditions acting on the mucous membrane. The former starts in autumn when equinoctial gales are blowing, and gives way to the other as the end of March begins to go out like a lamb; but the "swollen-down" time will not completely have established itself until the coming of the sweet May flowers. This seasonal distinction varies with the alterations of the years. The change may not come until the beginning of November, after a St. Martin's summer. It may turn again early in February if there is open weather at that time.

The winter swelling.—As a result of the swelling all lumens are narrowed and, when a clinical infection supervenes or is superimposed, drainage is held up as the acute phase passes away; and so the secretions which form the great characteristic of inflammations in this area cannot get away; they puddle and become infected. This causes a further swelling of the mucosa and they puddle the more. The sites of diminished lumen are the nose and nasopharynx in the main channel, and in the blind diverticula the openings of the nasal sinuses, and the whole Eustachian tube as regards the ear. The

subepithelial lymph nodes also swell. Thus the nasopharynx becomes blocked, and the posterior pharyngeal wall is studied with small masses of lymph tissue; the tonsils also swell from the organisms swept down to them by the ciliary action in the nose. If this first line of lymphatic protection is insufficient the second line comes into play, and one or many of the lymph nodes in the neck become palpable.

None of these things is cause for alarm; they are but the physiological reaction of the body to infection. They are concentrated at the head end, because it is here that all but a few infections enter the body other than those caused by wounds or bites. They should not be interfered with; they will pass with the passage of time, and with the coming of the milder weather.

Drainage.—They may be assisted by physiological drainage and by increasing the circulation to the parts primarily affected. Physiological drainage is obtained by nose-blowing, by hawking, and by spitting. There is nothing objectionable in this treatment when not done in public; in the privacy of the bathroom no-one will mind doing it. The nose-blowing should be performed systematically and efficiently. System can be obtained by regularity at stated times, just as we give medicine. Efficiency is obtained by blowing each side separately and continuing until it is heard that the nose is empty. If the secretion is sticky and very profuse it may be assisted away with warm saline solution introduced from the cupped hand or from a syphon douche.

Exercise.—The part primarily affected is the mucous membrane. There is one way and one way only of increasing the blood supply to this tissue, that is to boost up the whole circulation by exercise. This should be introduced gradually soon after the patient is out of bed. For all except the aged, skipping is the exercise of choice. It can be done in any ward and in most rooms in a house; if these are too small, in the passage. The exercise can be regulated so as not to tire the patient. My own practice is to prescribe two skips with both feet, two with one, two with the other, then two again with both feet. These exercise the brain and balance as well as the body. Further, they usually end with shrieks of laughter, and this again increases the circulation through the mucous membranes and helps the elimination of secretion.

Eustachian drainage.—When the ear is affected, laughter has a further value. It secures Eustachian drainage. This depends upon the movement of the palate, and this movement is provoked by laughter more than by any-thing else. After that perhaps comes chewing, and then talking. Now what-ever else is done for an inflammation of the middle ear cleft, operative or chemotherapeutic, the final recovery depends upon Eustachian drainage, and everything that can be done to secure this is essential to the treatment. Of the complications of inflammations of the upper respiratory tract none is more influenced by the seasons than the aural. Anybody can "cure" a case of otitis media in September: it requires great art to do so in January or February. The cure is physiological.

CHILBLAINS

By J. E. M. WIGLEY, M.B., F.R.C.P.

Physician for Diseases of the Skin, Charing Cross Hospital; Physician, St. John's Hospital for Diseases of the Skin.

As chilblains are one of the commoner of
> "the thousand natural shocks
> That flesh is heir to",

especially in damp and cold climates, and as their cause is not unconnected with good and varied nutrition and adequate warmth, this is an apt time for an article on the subject. Chilblains have evidently been recognized for many centuries, as their name—chill plus blain (O.E., blegen "an inflamed sore on the skin")—implies. The more usual technical term, erythema pernio, also indicates the essental lesion, an erythema, whilst the French synonym is *engelure*, and the German *frost-beule*.

As Pautrier (1936) put it, chilblains are an "apanage" (or lot) of childhood and adolescence; frequent between the age of five and fifteen years, rare after twenty, and exceptional after thirty. The victims are nearly always found to have cold extremities, "acroasphyxia". Barber (1926) has described two types of patient particularly liable to chilblains: there is the fat, phlegmatic, somewhat obtuse girl or woman with rough dry skin on the arms and legs, of a bluish colour and cold from the knees downwards; there is also the thin, highly strung, nervous type with marked vasomotor instability and tendency to blueness and coldness of the extremities. This latter type is usually subject to "colds" and liable to develop tuberculosis. In addition to these types, which may be considered as examples of endocrine imbalance, there are many cases in which physical examination can demonstrate no real variation from the normal. It is not without considerable interest that females are more often sufferers than males.

CAUSAL FACTORS

Cold, and especially the damp cold of northern latitudes, is a very important factor in the development of the chilblain. It is known that slight cooling of the skin causes a contraction of the capillaries, venules and arterioles, and that more extreme cold causes a dilatation of the small vessels and a contraction of the larger arterioles. The defective peripheral circulation (acroasphyxia), whatever its underlying cause, is more vulnerable to these conditions, resulting in the erythematous lesions known as chilblains, which are an *"érythème de stase"*, as aptly pointed out by Pautrier. It is very likely that the constant variations in atmospheric temperature which are so characteristic of what may be called the "chilblain latitudes" are really more active in provoking the lesions than the absolute degree of coldness present at the time. I have always understood that chilblains were almost unknown

in Arctic zones where frostbite is well known, but I have not been able to obtain authentic evidence of this. Wrong (1943) states that the chilblain "is becoming rare among urban dwellers (presumably in Canada) because of the introduction of central heating".

How far conditions of *general nutrition* can be held responsible for the incidence of chilblains it is difficult to be dogmatic about. It is quite obvious that even a mild degree of underfeeding must have its effect on the already vulnerable vessels of the acrocyanotic, but which part of the diet can be held responsible, whether the proteins, fats, carbohydrates or vitamins, is quite unknown. I know of no series of investigations which have given any consistent results. The calcium content of the serum, a remarkably constant one, is frequently held to be at fault, but I have not been able to find any real evidence of this, and the complete lack of success from the therapeutic use of calcium is too well known to need repeating. The nutritional basis of chilblains must be one which affects the balance of foods and their metabolism, and chilblains can be just one more example of the truth stated by St. Paul and so often overlooked: "If one member suffers, all the members suffer." Chilblains are essentially a winter affliction, although in a few individuals they may continue in the summer. Relapses are the rule and there is quite often definite evidence of an inheritance of the tendency.

DIAGNOSIS

The sites of election are the fingers, the ulnar sides of the hands, the great toes, the feet about the region of the heels, and the ears. Sometimes the nose may be affected and much more rarely the cheeks. The lesions may be single or multiple, are often bilateral and occasionally symmetrical. They may remain discrete, or may coalesce to form irregular swellings.

First degree or "simple" chilblains.—They first appear as erythematous macules, round, oval or variable in shape. They may be a livid red, violaceous or bluish in colour. The skin is shiny and appears thinned. The colour disappears on pressure and palpation gives an impression of infiltration. There is a sensation of discomfort, even pain, smarting, itching, engorgement, cramp and marked coldness. Changes of temperature, especially warming, exaggerate all these symptoms. The condition may clear in a few weeks with some slight scaling, but relapses are the rule.

Second degree or "broken" or ulcerated chilblains.—Here the swelling is more intense, the erythema more pronounced, producing mottled and livid plaques, and finally the epidermis "revolts" and ulcerates. Cracks and fissures about natural folds secrete a sero-purulent liquid. The lesions are very painful and sometimes develop blisters and crusts under which irregular ulceration may develop, even involving underlying cartilage. This ulceration usually heals with difficulty, leaving scars of varying degree. In severe cases mutilation of fingers, toes and ears may occur.

The *differential diagnosis* from lupus erythematosus and various forms of tuberculide may be extremely difficult. There may be certain abnormal

aspects which blur the frontiers between the conditions. There are ambiguous lesions, purplish erythemas, arranged like lozenges or little plaques, with slight scaling producing the type of lupus erythmatosus "*au début*". It may well be necessary to wait for the appearance of undoubted lupus erythmatosus on the face. Lesions may present a slightly nodular and vaguely necrotic centre very like papulo-necrotic tuberculides. As a rule the presence of characteristic dry "carpet tack" scaling with flat atrophic scarring without ulceration, and persistence through the warm weather, indicates lupus erythmatosus. Discrete, bluish nodules, small white scars without ulceration and bilateral symmetry, are signs of papulo-necrotic tuberculides.

Another condition which occurs in young women who are subject to chilblains is Bazin's disease, "*érythème induré des scrofuleux*", to use Bazin's original terminology. Indeed the two conditions may coexist, and it is doubtful whether lesions on the hands and ears, which have been described as Bazin's disease, are papulo-necrotic tuberculides or suppurating or necrosing chilblains (MacLeod, 1920). Bazin's disease is essentially a bilaterally symmetrical tuberculous affection occurring chiefly in the legs of young women. The sufferers are usually of heavy build, slow movement, sallow or definitely scrofulous. The lesion can first be felt as a painless subcutaneous thickening, about the size of a pea, over which the skin may be slightly reddened. The lesion gradually enlarges, assumes a livid colour and undergoes necrotic changes with formation of an ulcer. The ulcers may coalesce, forming an irregular area which heals slowly and with considerable difficulty. Other evidence of tuberculosis is usually present.

TREATMENT

It cannot be insisted too strongly that the best treatment of chilblains is prevention. The innumerable remedies of all kinds are an indication of the lack of universal success and emphasize the fact that there is as yet no specific remedy, either local or general.

The general management of the child with "chilblain circulation" (acrocyanosis) is most important. The general health should be looked after, and it is still very doubtful if there is anything better than cod-liver or halibut oil, with the addition of iron if there is any evidence of anæmia. Suitably graduated exercise is most valuable, plus a maximum of fresh air. The clothes should be warm, over the whole length of the limbs, the boots thick and the gloves loose in cold weather. Cold baths should be avoided as well as washing the hands in quite cold water. Tepid water, not hot, should be substituted, and the hands and feet should not be toasted in front of a fire or radiator. If the feet are clammy or sweaty, socks should be changed frequently, the feet washed in weak potassium permanganate solution and kept dry by dusting with talc powder. Should chilblains have developed, local treatment should be directed towards soothing and alleviating the symptoms and astringing the lesions.

Various sedative applications are effective, e.g., a lotion of lead and

opium or an ointment of carbolic acid and menthol, e.g.

℞ Carbolic acid .. .. .. 5 minims (0.3 c.cm.) ·
Menthol .. .. 5 grains (0.32 gm.)
Anhydrous lanolin .. .. ½ an ounce (15 gm.)
Soft paraffin.. .. .. to 1 ounce (31.0 gm.)

These should be applied continuously after bathing the chilblain with warm water and then drying.

Ichthyol is a useful astringent and may be applied as a paint as follows:—

℞ Ichthyol .. .. 60 grains (4 gm.)
Tannic acid .. .. .. 60 grains (4 gm.)
Resorcin .. .. 60 grains (4 gm.)
Water .. .. .. to 1 ounce (28.4 c.cm.)

or as the following cream:—

℞ Ichthyol .. .. 60 grains (4 gm.)
Calamine lotion
Anhydrous eucerin .. āā 1 ounce (31.0 gm.)

Iodine has many advocates and is frequently effective, especially as collosol iodine oil.

Ulcerated or broken chilblains will almost certainly require some antiseptic application to begin with, and I have usually found that penicillin cream or paste (about 250 units per gm.) is most effective in cleaning away the sepsis. It is seldom of any advantage to continue with this after about a week. A simple boracic ointment or mercurial paste is effective :—

℞ Ammoniated mercury .. .. 5 grains (0.32 gm.)
Ichthyol .. .. 10 grains (0.65 gm.)
Zinc paste (Lassar) .. .. 1 ounce (31.0 gm.)

The local application of suberythema doses of ultra-violet light may be most helpful in healing the infected lesions. Relief of symptoms may at times be obtained almost dramatically by the administration of small doses of X-rays: 70-100 r at 80 k.v. at weekly intervals, watching the results carefully.

The general treatment of a patient who has developed chilblains follows on much the same lines as indicated in the management above. I must add that I have not found any of the so-called specifics of universal help, probably least of all calcium by mouth. In the fat, phlegmatic type described by Barber (1926), thyroid extract has usually been helpful, although some prefer a polyglandular preparation. Whether or not this is due to the knowledge that it is more difficult to miss with a shot-gun than with a rifle is perhaps not fair comment. I cannot say that I have had any notable successes with vitamins, either on the shot-gun or rifle principle, but they generally have a supreme advantage of doing no harm. General irradiation with ultra-violet light (light-baths) often seems to help these sufferers, but of course it is most essential to be sure that there is no contraindication to their use.

References

Barber, H. W. (1926): *Lancet*, ii, 1180.
MacLeod, J. M. H. (1920): "Diseases of the Skin", 1st edition, London.
Pautrier, L. M. (1936): *Nouv. Prat. Derm.*, 3, 836.
Wrong, N. W. (1943): *Canad. Ass. med. J.*, 48, 520.

WINTER AILMENTS OF THE OLD

By HUGH BARBER, M.D., F.R.C.P.

Consulting Physician, Derbyshire Royal Infirmary; Visiting Physician, Derby City Hospital.

THERE are certain structural changes characteristic of old age, such as loss of weight, inelastic skin and rarefaction of bone, which may be described as the anatomical basis of senescence or physiological old age. In a long life, however, there will have been injuries sustained by the tissues from infection or from metabolic poisoning, so that the pathological condition of senility is rarely the result of longevity alone. There is much truth in the aphorism that "man is as old as his arteries", but in healthy senescence the cardio-vascular system may be as free from pathological change as any other part of the system, and clinical experience suggests that the more dramatic disasters in the circulatory system due to wear and tear tend to occur round about sixty years of age. It was a late president of the Alpine Club who used to say : "Old age is a pleasant time if you respect its limitations". The art of knowing where to stop, but at the same time keeping on with suitable activities, may be one of the chief guides in achieving healthy old age. Individual variation is considerable; old is a relative term, but for discussing ailments, an average from the age of sixty-five to the years of decrepitude may be taken. In some instances senescence may be hastened by an illness, which in a younger individual would have left no after-effects.

WINTER HYGIENE FOR THE OLD

Tactile and painful sensibility of the skin are diminished in the elderly, but they are very sensitive to cold. On this account in winter, adjustments must be made to suit senile changes. The forearms, wrists and lower part of the legs need clothing not formerly required. Sleep tends to be elusive so that a warm bed, a hot-water bottle and even night socks may be indicated, because the best remedy for insomnia is restful lying awake. When an old man can take a snooze over the fire in his armchair he will take no harm from a little less sleep than formerly in the night. An afternoon nap is more likely to promote a good right's rest than the contrary.

Restlessness in the day-time, on account of the restricted activity which winter entails, may need some mild sedative in senility, which is usually more suitable than an hypnotic at night. This inactivity requires careful watching in those who have no indoor hobby. Turning on and off the wireless is not so beneficial as reading over again the books that are old friends, and these turn the mind towards a restful night. An interest for the mind must be suited to the individual; but, whatever it may be, the stimulus is there. Sir Humphry Rolleston wrote: "Nothing hastens old age more than idleness. An alert mind can exist in an infirm body".

THE RESPIRATORY SYSTEM

Infective coryza is perhaps less common in the elderly than in the young, but

tends to reach the trachea, which may set up an irritating cough. For this, a simple lozenge is useful or perhaps one of menthol and heroin. A linctus may upset the digestion and cannot be taken in small, frequent instalments. In convalescence, small doses of cod-liver oil are beneficial.

Chronic bronchitis, with associated emphysema, is more prone to develop and recur in the active years of life but later on it is more likely to end in broncho-pneumonia. What a family practitioner might with justification call a "bronchial cold", requires great care. Not only must there be confinement to the house, but day and night atmosphere must be warmed, although ventilated. It is the fashion nowadays to decry the old expectorant mixtures, but so many elderly people of both sexes have borne witness to their value that they still have a place in therapeutics. Sometimes the indication is clear that the bronchial secretion can be modified with benefit. On other occasions a cough may be associated with some clear, frothy expectoration which is the result of early cardiac failure. For the relief of cough it may be necessary to fall back on the principle of trial and error. Sir William Osler in his last illness wrote: "All bronchial therapy is futile —there is nothing my good doctors have not made me try, but the only things of any service whatever in checking the cough have been opiates— a good drink out of the paregoric bottle or a hypodermic of morphia". His note concludes: "I have a splendid nurse".

With chronic bronchitis and "winter cough" it is well to remember that senile pulmonary tuberculosis is not uncommon. From the point of view of the patient there is not much practical value in making the diagnosis. Treatment resolves itself into guarding against secondary catarrhal infections, but the danger of infection to other people must never be overlooked.

Pneumonia itself is a difficult problem. A true pneumococcal lobar pneumonia is rare and, in spite of modern bacteriostatic remedies, the outlook is very grave. Broncho-pneumonia secondary to bronchiolitis is a serious condition requiring the greatest care, but the most common form of pneumonia in old people is something more·in the nature of an infarct, related to vascular disease, which gives signs of lobar consolidation. Owing to the natural blunting of sensibility to pain this condition may be unsuspected, and in any event a rise of temperature is less evident in the elderly. This form of pneumonia is a good example of Charcot's dictum that in old people "the organs suffer in silence". Hæmoptysis, however, is sometimes in evidence. An old person of good general physique, who is carefully nursed, will often recover from such an illness, and perhaps make the reputation of a new remedy, whether it be antiphlogistine, a vaccine, a mixture of creosote and iodide, thyroid and permanganate or something more modern. It is the nursing that counts, and the practitioner deserves his enhanced reputation if he recognized early what may have been an insidious complaint.

The value of specific treatment of pneumonia in the elderly is not easy to assess. The sulphonamides may be disappointing. When the problem has been solved of keeping up the concentration of penicillin in the system with

only two injections in the twenty-four hours, this will be the remedy of choice for pneumonia in old people, whatever be the etiology. No doubt some cases which begin by way of infarct or congestion become infected, on which account a non-toxic bacteriostatic remedy is indicated.

Whenever possible, elderly people should be nursed in their own homes. This applies particularly to bronchitis and broncho-pneumonia. The most convenient form of alcohol is whisky. Its scientific value needs no assessment if it brings a comfortable feeling. The will to recover is all-important in any illness at any age. The practitioner must remember that an elderly patient may be quietly assuming that the allotted span is run and therefore needs to be told quite clearly that his illness is one from which he can recover.

Convalescence later in life may be slow after any illness. When the bronchi or the lungs have been affected it is imperative to guard against treacherous weather when first going out of doors. Mistakes are made perhaps most frequently at that time of the year which R. L. Stevenson described as "our worst winter which we call the spring". It would be evading the issue to suggest that the elderly should spend their declining years where the rigours of winter are less severe. Quite apart, however, from financial and other considerations, it is important to remember that a time comes in life when it may be unwise to be uprooted from familiar surroundings.

THE CARDIOVASCULAR SYSTEM

Winter climatic conditions have considerable influence on the circulatory system, although it is more in the nature of inability of the inelastic arteries or the senile myocardium to react to change in temperature than of actual disease. "Dead fingers" or chilblains may recall the minor ailments of childhood, although rather ruefully an old man may say that he cannot now carry out the prescription of a run round the playground.

Angina of effort may come to light because of the added strain to the circulation of cold, and particularly when facing a cold wind. So also myocardial weakness will not stand up to a strong wind and an overcoat. It is common knowledge that *coronary thrombosis* in the very old may be attended with little or no pain, but this has no particular relation to winter. I cannot, from my own experience, say that *intermittent claudication* is worse in winter; both this condition and gangrene are more dependent upon the actual amount of arterial disease.

INFECTIVE CONDITIONS

With the restricted life of the elderly some infections are uncommon. *Influenza*, however, does reach them, although it is most likely to be brought into the house by someone else. It is a dangerous disease in old age. Convenient as the modern electric stove may be, it tends to give a badly ventilated atmosphere, which encourages the infection to spread through the house. Influenza is a good example of the insidious nature of disease later in life, because there may be signs of pneumonia without warning symptoms.

It is well to remember that a grandparent may pick up *whooping-cough*.

Herpes zoster ranks high as a disease which may undermine the strength of an old person for a long time. With advancing years this disease tends to be more severe and the intercostal nerves do not "suffer in silence". It is, of course, more probable that contact with herpes zoster should lead to chicken-pox rather than contact with the latter set up herpes; but I have met with this event.

Pyogenic infections, such as erysipelas or boils, are fairly common, tending to develop towards the end of winter. An old man when he passes the dark days of December may feel that he is going to enjoy another spring, but most old people find life trying, with vitality at a low ebb, towards the end of January, and I knew one old lady who claimed, year by year, to suffer from "Februaryitis".

. When there is a tendency to *cholecystitis* or to *cystitis* all the comforts of a home are important, including warmth in the bath room and for dressing. Too much attention should not be concentrated upon the action of the bowels, but here again comfort and warmth are indicated in dyschezia.

CHRONIC DISABILITIES

One of the aphorisms of Hippocrates runs as follows: "Old men generally have less illness than young men, but such complaints as become chronic in old men generally last until death". The progress of medical science has modified this point of view. We do not nowadays speak about the "catheter life". Indeed with regard to an enlarged prostate the elderly man scores, because he tends to do better surgically than those ten or fifteen years his junior.

But *osteoarthritis* may be hard to bear throughout the winter. It is in a condition of this sort that every endeavour should be made to keep the mind alert. The simple remedies will be the most valuable, both medicinal and physical. In that interesting correspondence *The Pollock-Holmes Letters*, Mr. Justice Holmes, aged ninety years, sent the following note to his friend: "I stoop but I haven't lumbago. The doctor said little processes like icicles had grown from my spine, and there was nothing to do but grin and bear it. Don't you wish you had icicles growing from your vertebræ?".

That is the wise cooperation which must be achieved between patient and doctor. Such a spirit must be encouraged in the hospital out-patient or in those who live in poor surroundings. Food that can be enjoyed and digested, a coal fire, a pipe of tobacco and mental interest suited to capacity, will help spondylitis deformans more than anything sold by the chemist.

THE ART OF THE GERIATRICIAN

Wise physicians have written of the medical aspects of old age. There is much recorded evidence of a scientific nature: for example, in one series of autopsies on patients seventy-seven years of age the cause of death in 36 per cent. was related to the circulatory system, in 24 per cent. to the respiratory,

and in only 13 per cent. to malignant disease. We can, if we wish, claim to have a speciality in geriatrics. But is it worth while? Is it not better for the family practitioner and other clinicians to treat and advise the elderly as part of their daily round?

The art comes with the correct psychological approach. The old man wishes to feel that he can progress in some direction, however little, and the old woman that she is of help to others. Relatives are apt to overlook these points of view; but a good doctor should have enough imagination to understand. It is possible that we hear a little too much about the dangers of frustration in the child. There will be many frustrations later, in adult life, for which some preparation may be beneficial. But year by year when a man is losing his old cronies and suffering from what Weir Mitchell called the "arctic loneliness of age", he will not push himself forward in the face of opposition or discouragement. His remaining talents will suffer and his health deteriorate if those around write him off as of little or no significance.

It is noticeable sometimes that an old man is not at his best in hospital. You may think that you are looking at a Parkinsonian countenance, and behold, if you ask him some question which gives him the opportunity of bringing his experience of life to bear on some modern problem, you may find an active brain well worth keeping in order.

A family practitioner must know senile psychology. When he first goes into practice he is apt to think that the elderly would like an older doctor. It is true that some patients have more or less grown up with an old friend who has been their medical adviser, but there is nothing they appreciate or need so much as a young medical mind (sometimes on shoulders not so juvenile) which is respectful, cheerful and understanding. Success may be estimated by the simple test as to whether the doctor himself enjoyed the interview or visit. For this end, it may be necessary to elude gracefully some symptom for which the indications for relief are not very clear, but the patient of either sex will be happy and better for the visit if something remains which recalls the best aspirations of the past. C. E. Montague wrote, "Nobody can easily believe that the winds of emotion ever blew quite such great guns in the heart of his father, or of his uncle, as they have done in his own". A hint occasionally of what you might have done as boys together, or for that matter as boy and girl, is not without curative value.

Time may bring the specialist geriatrician, but if the patients have their choice they will seek a family practitioner who has some reputation in treating their grandchildren, because they know he will not waste their time or money on a display of treatment for some condition for which medical science can only advise that the art is to "grin and bear it".

Some ailments develop in old people as the direct result of winter and others are more difficult to bear than in the summer months. A wise doctor will not presume to preach a sermon, but he must lead his elderly patients to understand that he knows the hard facts of existence, but theirs is the benefit if they find the spirit to carry on.

WINTER AILMENTS IN INFANCY

By CHARLES McNEIL, M.D., F.R.C.P.

Professor-Emeritus of Child Life and Health, University of Edinburgh.

UNDER this title an account will be given of those minor disorders of infants that are more prevalent in these Islands from September to April. To the winter season itself is added its approaches in autumn and its lingering departure in spring.

The subject of all the ailments that beset the life of infants from birth to the end of the second year is vast, important, and neglected. It is important because many of these ailments, especially the minor infections and disorders of the alimentary and respiratory tracts, disregarded or overlooked by mothers, become chronic, and lower the standard of health not only during childhood but throughout life. The corner of this wide field of infant ailments marked off by the word "winter" (the influence of climate and temperature) excludes the minor dyspepsias of infants, and includes the infective catarrhs of the nose, throat and middle ear, and the milder forms of rickets and spasmophilia. The winter season has little effect in producing this group of catarrhal disorders in the first six months of life, but after the age of six months, and until the end of teething about two years later, winter, and especially its beginning and end, does favour the incidence of this catarrhal group; also it is in the depths of winter and in early spring that a larger number of cases of rickets and spasmophilia are usually seen.

Winter, considered as the influence of lowered temperature or of abrupt changes from higher to lower temperature, has little or no effect in itself in producing upper respiratory catarrh in the younger infant lying secure and warm in his cot or in his mother's arms. After the age of six months, however, there are changes in the infant's way of life which expose him to the attack of infection: crawling and walking, his skin is more easily chilled; he now puts more infected material in his mouth; his gums congested with erupting teeth spread congestion into the fauces and throat; and it is probable that the process of calcification of the bony skeleton, which becomes more active at this period of life, tends to lower the level of calcium in the blood and to depress the vitality of the surface mucosa. In this concatenation of circumstances of the infant's life environment and constitution, the chilling of the skin by cold plays its part and is an important link in the chain of causes that produces year by year this seasonal crop of respiratory catarrhs in infants between the ages of six months and two years. In a recent public address (unpublished) Sir Alexander Macgregor, referring to his experience as Medical Officer of Health for Glasgow, said that each spring he looked for a rush of cases of measles and broncho-pneumonia punctually "with the arrival of the crocuses and daffodils".

CATARRH OF THE UPPER RESPIRATORY TRACT IN INFANTS

These catarrhs are the counterpart of the "common cold" of childhood and later life: they vary in degree and in the area affected; they produce obvious symptoms of nasal discharge, sneezing and cough, with general effects of malaise and fever; they may, and often do, coincide with teething; on the other hand they may be allergic in character and lead to infantile hay fever and asthma; or they may be the prelude to measles and whooping-cough, or essential bronchitis and broncho-pneumonia. Here, however, only the type of minor infective catarrhs affecting the nose and its accessory sinuses, the throat and the middle ear, and the larynx and trachea, the "infections banales" of French writers, will be dealt with. The actual illness is usually neither severe nor prolonged and does not require special treatment.

Chronic nasopharyngeal catarrh in older infants.—Acute catarrhs of the nose and throat, and of their accessory channels and cavities, are trivial and as a rule quickly pass off. But often enough they become a chronic catarrh of the nasopharynx. This chronic nasopharyngeal catarrh of older infants is in itself both trivial and unobtrusive, but it may be accompanied by complications which are serious. On the one hand it may lead to recurrent acute attacks or to the more serious complications of middle-ear catarrh, tonsillitis, bronchitis and broncho-pneumonia; on the other hand it may be associated with chronic dyspepsia, mild anæmia and malnutrition. Therefore this mild chronic nasopharyngeal catarrh, usually overlooked and often neglected, deserves careful and thorough treatment. The symptoms, although unobtrusive, are characteristic. There may or may not be nasal discharge, but there is nasal stridor indicating blockage of the nasal passages with mucus, and a tendency to mouth-breathing; there is usually a loose cough, easy and not frequent, and due to the clearing of the larynx of mucus that has trickled down from the pharynx; and, lastly, there are various signs of chronic dyspepsia, and particularly poor appetite, due to the swallowing of mucus from the throat, and minor degrees of malnutrition, anæmia and weakness. It is this condition of general slight deterioration of health, and of an area of infection in nose and throat, that carries a constant threat of some acute explosion of infection in the middle ear and mastoid, the bronchi and the lungs. Indeed, every case of chronic nasopharyngeal catarrh in this age period of infancy (six months to two-and-a-half years) is a potential broncho-pneumonia. This is the age period of broncho-pneumonia, and it is a reasonable opinion that most cases of broncho-pneumonia, including those in measles and whooping-cough, are preceded by this common mild ailment of chronic nasopharyngeal catarrh.

The *treatment* is twofold: the cleansing of the affected area in nose and throat, and attention to the digestive disorder. How can the nose and throat of an infant of one year old be cleared of mucus and the underlying mild catarrh cured? Not by the swallowing of 'drugs, but only by their local application in solution to the affected surfaces. Throat paints and gargles are

impossible at this age. The use of droplet sprays is possible but often not practicable. There remains the use of solutions dropped into the nose and the painting of solutions on the tongue and palate. These methods of local application are quite well tolerated by infants, and their persistent regular application is effective in clearing the surfaces of mucus and restoring a healthy mucosa. They may be described as a daily nasopharyngeal toilet. Glycerin solutions are the best: indeed glycerin alone, diluted with water 1 in 5, is most satisfactory, or the soothing and very mild antiseptic action of thymol [compound glycerin and thymol (*B.P.C.*) in 2 or 3 parts of water] may be added to the glycerin. I have not found the carbolic acid glycerin so effective. At a later stage, when the mucous scum has been removed, the astringent action of diluted tannic acid glycerin is useful, or the use of light liquid paraffin, but the first glycerin solutions may be used throughout, remembering, however, that they should be used twice or thrice daily and continued for several months. Painting of the tongue and palate with similar solutions should also be carried out.

The second part of the treatment, dealing with the effects in the alimentary canal and with the general condition, is also important. The following prescriptions are recommended. Once daily for a fortnight, give half-an-hour before the first meal, one teaspoonful of milk of magnesia in 2 ounces (57 c.cm.) of warm water and follow by a light breakfast of diluted sweetened milk and a little thin toast and jelly. Also thrice daily during the fortnight give (preferably before meals):—

℞ Compound tincture of rhubarb .. 5—7 minims (0.3—0.4 c.cm.)
   Syrup of orange .. .. .. 15 minims (0.9 c.cm.)
   Compound infusion of gentian .. 60 minims (3.6 c.cm.)

This combination of drugs is designed to clear mucus out of the stomach and alimentary canal, to restore appetite, and to keep the bowels open. It may be necessary to repeat this treatment of dyspepsia several times after suitable intervals. If anæmia is present, a course of iron should be given, for example, Quevenne's iron, 1 grain (65 mgm.) t.i.d., the powder being added to the food.

This condition of chronic nasopharyngeal catarrh in infants is trivial in itself but has immediate serious results in disturbing digestion and lowering nutrition, and it is often the precursor of serious and fatal diseases both in the upper and lower respiratory tract; for this reason it well deserves attention and careful treatment. It is not confined to, but is common in, later infancy, and being especially common in winter it falls within the subject of this article. It is seldom mentioned in medical textbooks.

Teething troubles.—These certainly belong to infancy, but are unaffected by season or climate. If they do occur in winter, and if they are accompanied by mild congestion of the mucous membranes of the whole respiratory tract, as often happens, we have a morbid condition, allergic and not infective in origin, similar to that of acute infective nasopharyngeal catarrh. This is a

temporary and trivial ailment, but it is worth while dealing with it by a substantial reduction of food for two or three days, by an increase of fluid, and by the use of mild aperients.

Laryngitis and tracheitis.—In the acute phase of nasopharyngeal catarrh, the catarrh may spread down to the larynx and trachea, and this spread will be shown by a huskiness of voice and cough or by a resonant baying cough. Also, laryngeal catarrh may be accompanied by spasm, with the features of croup. This extension of catarrh is seldom serious, and it is easily and effectively treated by the application of poultices (antiphlogistine) to the neck and throat, and the moistening of the air by a steam-kettle. Sometimes chronic catarrh remains after the acute attack, not in the larynx, but in the lower part of the trachea, where it produces a loud barking cough which is apt to become paroxysmal and very troublesome shortly after bedtime. This, however, has no special prevalence in winter and, uncommon at any time, occurs rather in later childhood than in infancy; when established, it is an inveterate condition, difficult to cure.

RICKETS AND SPASMOPHILIA

Both these diseases are disorders of calcium metabolism, a deficiency of lime salts in the bones and in the blood plasma respectively; both occur more often at the end of winter and in early spring than at other times, and both occur almost entirely between the ages of six months and two years. When pronounced, they are major diseases, but their first symptoms might be called minor ailments and may therefore be considered here.

Rickets in its early or mild form produces muscular softness and lethargy of the limbs and trunk, and too free perspiration; later, the soft bony swellings in the skull, ribs and long bones, and delay in the cutting of teeth. The muscular indolence is an essential and early feature, and one easily noted if looked for; the bony changes are less easy to be sure about by clinical observation, but can be definitely determined by X-ray examination.

The treatment should be as thorough as that given to established rickets: increase of milk in the diet and reduction of cereal and other starches; the free use of egg-yolk and fish-liver oils; the administration of vitamin D; the free exposure of the child to the winter air and sun, and a course of ultra-violet irradiation.

Severe rickets has become a rare disease: it is even doubtful if mild rickets occurs to any extent; but the conjunction of winter darkness with a diet that is faulty, will produce substandard conditions of health that can be easily remedied by the measures described.

Spasmophilia.—If recognizable rickets has almost disappeared from the clinical map, what can be said of its first cousin, spasmophilia, sometimes called nervous rickets? Spasmophilia is the clinical expression of a low level of calcium salts in the blood plasma, and shows itself in one or more of three ways: sudden attacks of laryngeal spasm (laryngismus), prolonged spasm

with swelling of the hands and feet (tetany), and general convulsive attacks. Spasmophilia was never common, but it still remains, and has to be recognized, understood and treated. *Tetany* is a painful and obvious condition, and is not a minor ailment. But mild attacks of *laryngismus*—a sudden check in breathing followed by a crowing inspiration—are easily overlooked; these are seasonal, occurring in winter or spring, and they are only met with in infants between six months and two years. *Convulsions* will not be overlooked but may well be misunderstood. For both these types of spasmophilia (laryngismus and convulsions) the clinical test of facial irritability—Chvostek's sign—provides easy and certain diagnosis, and for both the treatment is similar. Soluble calcium salts must be given to raise the calcium content in the plasma; either intramuscular injections of 10 per cent. calcium gluconate, 5 to 10 c.cm., daily for a week, or oral doses of calcium chloride in solution of syrup, 5 grains (0.32 gm.), thrice daily for a week. The diet must also be anti-rachitic, as detailed above, and a regime of open air and sunshine instituted. In the event of convulsions, sedative treatment with phenobarbitone, ¼ grain (16 mgm.), thrice daily for several weeks, should be given after the blood calcium level has been restored.

Spasmus nutans.—This rare condition occurs only in infancy, and usually in early infancy; it is a disorder of winter and darkness, producing a slow shaking or nodding of the head along with rapid nystagmus. The condition is trivial and will pass of itself. The treatment is to give the baby light and air and correct any faults in the diet.

SUMMARY

A group of winter ailments in infancy has been described. The more important members of this group are:—chronic nasopharyngeal catarrh, the milder forms of rickets, and spasmophilia. All these minor illnesses are uncommon in the first six months of infancy, but they are common in older infants and especially in the winter season. Those mentioned above may occur singly or in combination.

Chronic nasopharyngeal catarrh is the most important member of this group, because it is often the precursor of serious acute infections in every part of the respiratory tract, such as acute otitis and mastoiditis, tonsillitis, bronchitis and broncho-pneumonia. But the whole group deserves the attention and care of medical practitioners. They are the result of a combination of circumstances, the instability of the changing physical constitution of older babies, faults in diet and regime, bacterial infection, and also the peculiar deficiencies of the winter climate of the northern hemisphere. These minor illnesses are no doubt trivial in themselves, but they are loaded with the potential of much chronic illness and many deaths.

LOW BACK PAIN AND SCIATICA

By A. S. BLUNDELL BANKART, M.Ch., F.R.C.S.

Consulting Orthopædic Surgeon, Middlesex Hospital.

IN recent years, apart from war wounds and fractures, few subjects in orthopædic surgery have attracted so much attention as "low back pain" and sciatica. The causes of pain in the back are many and various, but certain conditions which are common in orthopædic practice can be readily recognized. If you stand these patients up in front of you and say to them "where is your pain?", they will automatically separate themselves into five groups.

CLASSIFICATION

(1) The largest group will indicate quite accurately the posterior superior spine of the ilium which overlies the centre of the sacro-iliac joint. On pressing with the thumb over this point, the patient will wince or exclaim and, although there may be some superficial hyperæsthesia around it, there is little difficulty in establishing the fact that this is the principal seat of the pain. There is often pain referred to the outer side of the thigh and the groin, but *not* down the back of the thigh. The X-rays are normal. This is *sacro-iliac strain*, the most common cause of persistent pain in the lower part of the back. It is especially common in women, in whom it often follows child-birth or gynæcological operations, or it may be caused by a twist or a fall. The great majority can be cured by manipulation under an anæsthetic, and those who are not so cured can be cured outright by arthrodesis of the sacro-iliac joint.

(2) A smaller group will draw their fingers horizontally across the back just above the sacrum, and say that the pain is there. These cases are of two types:—(a) Pain and tenderness are definitely localized to the tip of the spinous process of the fifth lumbar vertebra and the space immediately below it. Forward flexion of the spine is free, but sharp pain is felt on hyper-extension. There are no other symptoms or signs. This is *lumbo-sacral strain*. Most of the patients are women, many of whom have prominent abdomens and exaggerated lordosis. The condition does not respond to manipulation. It may be relieved by a belt, which incidentally is an abdominal and not a spinal support. Persistent cases can be cured by division of the ligaments attached to the spinous process, and the simplest way of doing this is to excise the process. (b) In the second type the pain is more diffuse and more aching in character. There is stiffness of the lower lumbar spine and pain on forced movements. The X-rays show arthritic changes in the lumbo-sacral joints. It may be due to injury, possibly of the intervertebral disc, or it may be associated with congenital anomalies of the lumbo-sacral region. These patients may obtain some relief from physiotherapy or, failing that, from a spinal support, but the only permanent cure is a spinal fusion.

(3) The third group will indicate a point over the erector spinæ muscle on one or other side. There is deep tenderness on pressure over that point and spasm of the muscles. If the patient can bend forwards at all, he inclines the body to the affected side so as to avoid stretching the muscle. In acute cases there is diffuse hyperæsthesia over the whole back and half-way down the back of the thighs. In chronic cases there is a variable degree of hyperæsthesia in addition to the local pain and tenderness. The condition comes on suddenly with a sharp stabbing pain in the back while lifting something or while stooping in an awkward position. This is succeeded by a dull ache and further sharp stabbing pains on movement. It is perhaps the most disabling of all trivial injuries and frequently there is a considerable degree of neurosis added. It is due to rupture of some of the deeper fibres of the erector spinæ muscle and the proof of this is that occasionally, although rarely, a piece of bone is pulled off from one of the transverse processes by the violence of the muscular contraction. The treatment of both acute and chronic *lumbar back strain* is to mobilize the back as soon as possible: in acute cases massage and exercises as soon as the patient can tolerate them; in chronic cases manipulation under an anæsthetic followed by massage and exercises. This practically always cures the condition, except when there is a compensation neurosis present. Immobilization of an acute back strain turns it into a chronic one; immobilization of a chronic back strain perpetuates it indefinitely.

(4) The fourth group, when asked to localize their pain, will point to the upper part of the buttock and on investigation it will be found that the point of maximum tenderness is not over the posterior superior spine, but about an inch-and-a-half below and to the outer side of it, i.e., over the great sciatic notch. These two points are anatomically close together, but clinically they are miles apart and there should be no difficulty in distinguishing between them. The pain goes down the back of the thigh and leg and it may reach the foot—in fact, these patients have *sciatica*. They may or may not complain of pain in the back; but whether they do or do not, they will practically always be found to have stiff lumbar spines, spasm of the erector spinæ muscles, and pain on forced movements. These cases will be referred to again later.

(5) Lastly, there is left a group of cases which have nothing in common except that they do not fall into any of the preceding groups, but they all have sufficiently distinctive features of their own. Here are cases of diffuse osteoarthritis, ankylosing spondylitis, spondylolisthesis, old crush fracture, tuberculous disease, and secondary growths, and it need hardly be said that routine X-ray examination is of paramount importance in their diagnosis.

It must be remembered that practically every case of long-continued pain in the back develops a neurosis in some degree, and sooner or later it "gets the patient down". It varies from a local hyperæsthesia of greater or less extent up to a profound neurasthenia. This superimposed functional ele-

ment must not be allowed to obscure the diagnosis and treatment of the underlying condition.

SCIATICA

It remains now to consider sciatica in more detail, because recent work has, I think, tended to confuse rather than clarify the issue.

Sciatica is one of the classical diseases of medicine. For centuries it has been known to be mainly an affection of middle-aged and elderly people. It is characterized by pain in the course of the great sciatic nerve. The pain is felt in the buttock and down the back of the thigh and leg to the foot. It is described as a constant heavy gnawing sensation with or without acute ·exacerbations. There is tenderness on pressure over the great sciatic notch and in acute cases there is tenderness of the muscles of the thigh and leg. In chronic cases there is flabbiness and wasting of the muscles, and tactile sensation is impaired over the outer aspect of the leg and dorsum of the foot. In such cases the Achillis jerk may be diminished or absent, but otherwise the tendon reflexes are normal. The pain is increased by any movement which stretches the nerve, so that flexion of the hip with the knee straight is limited and painful, and the patient instinctively adopts an attitude of relaxation with the hip and knee slightly bent. The onset of sciatica is almost invariably accompanied or preceded by pain and stiffness of the lumbar spine, and many patients give a history of previous attacks of "lumbago".

For many years no-one doubted that this affection was due to neuritis of the great sciatic nerve, and some physicians still maintain that this is the only "true" sciatica. But there seems to be little doubt now that symptoms similar to those of the classical disease may be due to causes other than sciatic neuritis. At any rate, in current literature the term sciatica is now applied to any condition in which there is constant pain in the course of the great sciatic nerve or part of it.

When a neurologist is confronted with a lesion of a long tract in the central nervous system, his first concern is to determine its *level*, because he knows that in certain situations certain conditions are most likely to occur. Surely, the same applies to an affection of the longest tract of peripheral nerve fibres in the body. The great sciatic nerve is composed of fibres derived from the 4th and 5th lumbar and the 1st, 2nd and 3rd sacral nerves. There are at least five situations in which these fibres or some of them may be affected by pathological processes, i.e., (1) in the spinal cord (rarely); (2) in the nerve roots; (3) in the intervertebral foramina; (4) in the pelvis; (5) in the thigh.

The prolapsed disc.—In 1934 Mixter and Barr published an account of forty cases of sciatica proved by operation to be due to posterior protrusion of intervertebral discs. The prolapsed disc then became recognized as an occasional cause of sciatica, but constituting only a small percentage (3 to 4 per cent.) of the whole. Then came the war, and great numbers of young men and women were taken from more or less sedentary occupations and

put to strenuous work and physical exertion to which many of them were unaccustomed and perhaps unsuited. In these circumstances it is not surprising that many weak backs were discovered, backs which probably would never have been heard of in normal times. Prolapsed discs then became common, and soon it was confidently stated that *every* case of sciatica is due to a prolapsed disc. It has even been stated that everyone who has a pain in the back and spasm of the erector spinæ muscle has a prolapsed disc or is about to have one! This fashionable diagnosis has now become so firmly established that some surgeons cannot believe the evidence of their own eyes, and when no disc is found at operation they say that the patient has a "concealed" disc. This is dealt with by thrusting a blunt instrument into the back of an apparently normal disc and curetting out the nucleosus pulposus. Actually, many cases have been operated upon in which no disc has been found, and many more have been reported as prolapsed discs in which no operation has been done and therefore proof was lacking.

Nevertheless, the prolapsed disc is a definite clinical entity. Before the war it was diagnosed with reasonable certainty by intrathecal injection of lipiodol and X-ray examination; during the war lipiodol was not generally available and it became necessary to rely upon a clinical diagnosis only. When a comparatively young patient gets pain in the lumbar region during some lifting effort or on rising from a stooping position or perhaps after a fall, and this is followed immediately or soon after by pain in the distribution of the great sciatic nerve, there is at least a probability that he has a prolapsed intervertebral disc. He will be found to have stiffness of his lumbar spine, spasm of the erector spinæ muscles, tenderness over the great sciatic notch, and pain down the back of the thigh and leg. The pain is increased by coughing or sneezing. As a rule there is no tenderness over the trunk of the sciatic nerve or its branches; the muscles are not tender and there is little, if any, wasting; straight leg raising is limited, as it is in all cases of sciatica; the tendon reflexes are normal. X-rays of the lumbar spine may show narrowing of one of the two lowest intervertebral spaces or they may be normal. In many cases the protein content of the cerebrospinal fluid is raised. Such cases, if they do not recover quickly, should be operated upon. A laminectomy should be done and the prolapsed disc removed. The immediate result of this operation is a dramatic relief of pain; the late results have still to be assessed. It must be remembered that the intervertebral disc is only a part of the articulation between two vertebræ. Loss of a disc leads to approximation of the adjacent vertebral bodies and throws an abnormal strain upon the lateral joints and the ligaments connecting the posterior arches. This in turn may lead to arthritis of these joints, and the patient is liable to suffer from pain in the back at a later date. Therefore some surgeons believe that a spinal fusion should be done when a prolapsed disc is removed.

Spinal arthritis.—Turning back now to the classical picture of sciatica, I

would repeat that this is typically an affection of middle-aged and elderly people. It is more common in men than in women. Most of them have stiff lumbar spines, spasm of the erector spinæ muscles, pain on forced movements, often a tilt of the body towards the opposite side (so-called sciatic scoliosis), a history of previous attacks of "lumbago", and more or less evidence of osteoarthritis in X-rays of the lumbar spine. They have, in fact, symptoms which no orthopædic surgeon would hesitate to diagnose as arthritis, if they occurred in any other part of the body or even in the spine itself without sciatica.

The frequent association of spinal arthritis with sciatica was emphasized by Putti in 1927 and, although this view is not shared by the majority of orthopædic surgeons, I believe that this is the most common cause of sciatica seen in orthopædic practice. In 1915 the French neurologist, Sicard, drew attention to the liability of nerves to irritation or inflammation as they lie in bony canals or foramina, and he expressed the view that sciatica was a common example of this condition. In such cases the spinal nerves are affected as they lie in the intervertebral foramina practically in contact with the lateral intervertebral joints. It has never been suggested that the joints themselves or bony outgrowths from them actually press upon the nerves; indeed, gross enlargement of these joints is unusual. But it is suggested that the inflammatory reaction around the joints in arthritis is responsible not only for the stiffness of the lumbar spine, but also for the irritation or inflammation of the adjacent spinal nerves. It is perhaps significant that, with the exception of local injections into the nerve, nearly all the measures commonly employed for the relief of sciatica are also those which are found useful in chronic arthritis. These include rest in bed, immobilization in plaster, various forms of physiotherapy, especially heat, massage, exercises, and manipulation. It only remains to add that when these measures fail, persistent sciatica can nearly always be cured by excision of the lateral intervertebral joints (spinal arthrectomy). This operation opens up the intervertebral foramina behind and effects a "decompression" of the spinal nerves within them. Incidentally, it gives a perfect approach to the intervertebral discs, so that these can be examined at the same time.

Growths in the pelvis may cause severe sciatic pain from involvement of the sacral plexus; but these conditions can be excluded by routine pelvic examination. Uncomplicated sacro-iliac strain never causes sciatica, but *tuberculosis of the sacro-iliac joint* does in about 20 per cent. of cases. *Osteoarthritis of the hip* is given in all medical textbooks as a cause of sciatica, but I have never seen it as such. Patients with osteoarthritis of the hip, however, often have osteoarthritis of the spine.

Lastly, none but extremists will deny that *neuritis of the sciatic nerve trunk* does occur. It probably occurs quite often in milder degree. But the severe form of neuritis with marked tenderness of the nerve and its branches, wasting of the muscles, impairment of sensation, and altered tendon reflexes, is seldom seen in orthopædic practice.

ANÆSTHETICS IN OBSTETRIC PRACTICE

By A. D. MARSTON, M.R.C.S., D.A.

Anæsthetist, Guy's Hospital, and the Royal Masonic Hospital.

INDICATIONS for the use of anæsthesia and analgesia in obstetric practice are numerous, and may be divided into three groups:—

(1) During labour in (a) painless child-birth; (b) instrumentation, intra-uterine manipulations, expression of placenta, and perineal repair.

(2) Version of the fœtus.

(3) Cæsarean section.

PAINLESS CHILD-BIRTH

During the last decade both the lay public and the medical profession have taken an increased interest in this subject, and there is a growing recognition of the advantages that accrue both to mother and child from the achievement of this end. The general condition of the mother after a pain-free labour is superior to that following unassisted child-birth. The reasons for this are threefold:—

(a) Absence or diminution of psychic trauma.

(b) An average shortening of the duration of labour.

(c) A tendency to sleep between the pains of labour.

As regards the child, it has been stated recently (Cole, 1939) that the process of birth causes fœtal shock of some duration. If, however, the mother is anæsthetized during the actual parturition, this effect is reduced and, furthermore, the tendency to weight loss during the ensuing few days is diminished (Langton Hewer, 1944).

The means available for securing these advantages are numerous, but only those will be described which have won the approval of competent contemporary exponents of the specialities of anæsthesia and obstetrics.

The ideal requirements of any form of treatment are (a) immediate and efficient action; (b) no delay of labour; (c) no toxic effects on mother or child; and (d) no respiratory depression to hinder the immediate vitality of the newly born infant.

Before describing treatment in detail, three factors ancillary to this immediate result should be mentioned.

growing custom, particularly noticeable in the United and certain of the British Dominions, of attending institutions instead of in domiciliary practice, and the successful obstetric analgesia under such auspices

tional tendency is a recognition of the toxic and other of chloroform which, although for some time accepted been less readily recognized in obstetric practice.

The third factor concerns administrative personnel. In view of the fact that the majority of confinements in this country are attended by midwives, special methods have had to be devised to bring this treatment within their province.

The four essential factors in the modern technique of treatment in labour are:—(a) Antenatal instruction; (b) drug therapy; (c) the use of an apparatus to provide analgesia and anæsthesia; (d) local analgesia as an alternative to (c). The present tendency is to produce results by the *combined* use of these methods.

Antenatal instruction.—This is important, as clinical experience has shown that better results are obtained from a cheerful and cooperative patient who has received intelligent and sympathetic psychological preparation. The procedure for analgesia should be frankly discussed and certain points stressed, such as (a) the nature of analgesia, its safety and the importance of cooperation; (b) instruction in the use of an apparatus, and the fact that it is in the first instance self-applied (Minnitt, 1944).

Drug therapy.—This should be used in the first stage when definite signs of discomfort have become evident. Although it is possible to treat the entire labour with drugs, it is now realized that better results accrue from their use only in the early stage, preparatory to the employment of general or local analgesia, the effects of which are thereby enhanced, and uterine inertia, respiratory depression, excessive sleepiness and non-cooperation avoided. Analgesic drugs, which are numerous, may be used singly, but synergism, i.e., the employment of smaller doses of different agents, secures a safer and more efficient result.

The use of analgesia, amnesia and anæsthesia may be combined to obtain the best average of successful treatment. When an anæsthetist is available the production of surgical anæsthesia is a definite advantage during actual parturition, and until the placenta is delivered and any perineal repair completed.

ANALGESIC DRUGS

A well-tried and simple mixture is composed of potassium bromide, 20 to 30 grains (1.3 to 2 gm.), with chloral hydrate, 15 to 20 grains (1 to 1.3 gm.). Tincture of opium, 5 to 15 minims (0.3 to 0.9 c.cm.), may be added if required, and the dose repeated in four hours, if necessary. As this mixture tends to produce nausea, it should be well diluted if given by mouth. In the "District" practice of the Obstetric Department of Guy's Hospital it is customary to administer the mixture per rectum to avoid this nausea, and this method has worked well in the average case. The regulations of the Central Midwives Board allow the drugs mentioned to be used by midwives.

The Derivatives of barbituric acid: nembutal, soneryl, seconal and pentothal sodium.—Of these *nembutal* is perhaps the best known and most commonly used. It is contained in 1½-grain (0.1 gm.) capsules, of which two will usually

ANÆSTHETICS IN OBSTETRIC PRACTICE

BY A. D. MARSTON, M.R.C.S., D.A.

Anæsthetist, Guy's Hospital, and the Royal Masonic Hospital.

INDICATIONS for the use of anæsthesia and analgesia in obstetric practice are numerous, and may be divided into three groups:—

(1) During labour in (a) painless child-birth; (b) instrumentation, intra-uterine manipulations, expression of placenta, and perineal repair.

(2) Version of the fœtus.

(3) Cæsarean section.

PAINLESS CHILD-BIRTH

During the last decade both the lay public and the medical profession have taken an increased interest in this subject, and there is a growing recognition of the advantages that accrue both to mother and child from the achievement of this end. The general condition of the mother after a pain-free labour is superior to that following unassisted child-birth. The reasons for this are threefold:—

(a) Absence or diminution of psychic trauma.

(b) An average shortening of the duration of labour.

(c) A tendency to sleep between the pains of labour.

As regards the child, it has been stated recently (Cole, 1939) that the process of birth causes fœtal shock of some duration. If, however, the mother is anæsthetized during the actual parturition, this effect is reduced and, furthermore, the tendency to weight loss during the ensuing few days is diminished (Langton Hewer, 1944).

The means available for securing these advantages are numerous, but only those will be described which have won the approval of competent contemporary exponents of the specialities of anæsthesia and obstetrics.

The ideal requirements of any form of treatment are (a) immediate and efficient action; (b) no delay of labour; (c) no toxic effects on mother or child; and (d) no respiratory depression to hinder the immediate vitality of the newly born infant.

Before describing treatment in detail, three factors ancillary to this subject may be mentioned.

First, there is the growing custom, particularly noticeable in the United States, Scandinavia, and certain of the British Dominions, of attending labour in specialized institutions instead of in domiciliary practice, and the increased facility for successful obstetric analgesia under such auspices cannot be doubted.

Another international tendency is a recognition of the toxic and other undesirable effects of chloroform which, although for some time accepted in surgery, have been less readily recognized in obstetric practice.

Pentothal sodium.—Given by mouth, in an initial dose of 4 grains (0.25 gm.), this drug will speedily diminish or abolish discomfort in the first stage. A further 3-grain (0.2 gm.) dose may be given after thirty minutes, and again after another hour. This is usually all that is needed if inhalation or local analgesia is to be used for the later stages. If used alone, however, the 3-grain (0.2 gm.) dose may be repeated at hourly intervals until a maximum total dose of 20 grains (1.3 gm.) has been given. Scopolamine, 1/150 of a grain (0.43 mgm.) may be added to increase the effect of this treatment (Langton Hewer, 1944).

INHALATION ANALGESIA AND ANÆSTHESIA

Nitrous oxide and oxygen.—This is probably the best method available. With an intermittent-flow machine, a mixture of from 10 to 15 per cent. of oxygen with 85 to 90 per cent. of nitrous oxide will produce efficient analgesia in three to four average breaths. Between the pains the patient tends to sleep or be comfortably drowsy, this last effect being enhanced if suitable minimal drug treatment has been given in the early stages. The patient uses the apparatus herself until the late second stage, after which it is better for the administration to be taken over by the anæsthetist, the patient being encouraged to hold her breath and bear down *after* securing analgesia. With cooperation this stage will pass satisfactorily until actual delivery is at hand. Anæsthesia now replaces analgesia, and continues until the placenta is expressed and any perineal repair completed.

After minimal drug preparation this method is excellent, as the infant usually breathes readily, labour is shortened in the average case, analgesia is adequate, anæsthesia spares shock to mother and child, the uterus contracts well after delivery, toxic effects are absent, and the method is the safest at the anæsthetist's disposal.

There are special types of apparatus designed or adapted for this work, and I recommend either the McKesson or the "Portanest", which has recently been made available by the British Oxygen Company. The "Portanest" is light in weight, readily portable, and has the advantages of intermittent flow, physically correct calibration of oxygen percentage supply, known pressures of gaseous supply, graduated re-breathing, and an emergency oxygen supply under positive pressure.

Nitrous oxide and air.—This is a valuable alternative method for use by midwives and the occasional anæsthetist.

Minnitt's apparatus was introduced some twelve years ago and has the advantages of simplicity, portability, economy and safety. The machine delivers roughly 45 per cent. of nitrous oxide with 55 per cent. of air and, although not ideally efficient, has proved extremely useful. A series of over 3,000 administrations by midwives has been recorded with no mortality and a successful degree of analgesia in the majority of cases.   It is not possible

give relief in from twenty to thirty minutes. A further capsule (0.1 gm.) may be given after an hour and repeated, but on no account should a total dose of 7½ to 9 grains (0.5 to 0.6 gm.) be exceeded in twelve hours, lest cumulative action occur, with untoward results. Nembutal, 3 grains (0.2 gm.), may be usefully combined with chloral hydrate, 20 to 30 grains (1.3 to 2 gm.), and repeated after two hours if required (Langton Hewer, 1944).

Morphine.—A single hypodermic injection of morphine, 1/6 to 1/4 of a grain (11 to 16 mgm.), heroin, 1/12 of a grain (5.4 mgm.), or omnopon, 1/3 to 2/3 of a grain (22 to 45 mgm.), may be used at the beginning of the first stage. This will often provide comfort during the waiting period before inhalation analgesia, but should not be repeated, as it tends to prolong labour and depress the respiratory centre of the fœtus.

Hyoscine hydrobromide (scopolamine).—This will produce amnesia if used alone in a dose of 1/150 of a grain (0.43 mgm.), and may also be administered in combination with nembutal, syrup of chloral, or pethidine.

In the "twilight sleep" technique an initial dose of scopolamine, 1/150 of a grain (0.43 mgm.), is given with omnopon, 1/3 to 2/3 of a grain (22 to 45 mgm.), or morphine, 1/6 to 1/4 of a grain (11 to 16 mgm.). Thereafter, hyoscine, 1/400 of a grain (0.16 mgm.), is repeated alone at required intervals, but as this drug is a respiratory depressant contemporary practice favours its restriction to a single dose (Lloyd-Williams, 1941).

Pethidine (dolantin; demerol).—This is a welcome addition to the available drugs for it is a good analgesic, is free from toxic effects, and has no delaying action on labour. Cases of addiction to the drug have, however, been reported from the U.S.A. Intramuscular injection of 100 mgm. affords speedy relief from discomfort in the first stage, and the dose may be repeated after an hour. Pethidine may be combined with chloral, nembutal or scopolamine to secure enhanced effect, or if it is desired to carry out treatment without inhalation or local analgesia; but in my experience it is best used before inhalation technique as an efficient preliminary medication.

Bromethol (avertin; tribromethyl alcohol).—This drug administered per rectum produces a reliable basal narcosis and is especially valuable in cases of abnormal prolongation of the first stage. As it tends to cause respiratory depression and a lessening of uterine contractions it should be used in precise dosage of 0.075 gm. per kgm. of body weight.

Paraldehyde.—Although not so certain in action as avertin, this drug is preferable in the average case, as it has no depressing action on respiration and is more easily dispensed. Paraldehyde is mixed with normal saline to form a 10 per cent. solution, the dose being from 30 to 60 minims (1.8 to 3.6 c.cm.) per stone (6.9 kgm.) of body weight, with a maximum total dose of 1 ounce (28.4 c.cm.).

It is advisable to empty the lower bowel by an enema before injecting avertin or paraldehyde in a pain-free interval. If a pain occurs during injection, the buttocks should be held tightly together until it is over.

For these reasons chloroform should be employed only in the absence of more suitable methods, and not as a routine measure.

This drug may be administered on an open mask or by means of a Junker's bottle. Breakable glass capsules containing chloroform 20 minims (1.2 c.cm.) for use by midwives acting alone have been given a limited trial but their use is now largely abandoned.

LOCAL ANALGESIA

Spinal analgesia (sub-arachnoid block) is seldom employed, and is not recommended in labour, as its action interferes with the mechanical efficiency of the uterine muscles.

Caudal (extra-dural) block has been extensively used in America, but only to a limited extent in this country, where views upon its efficiency and desirability are by no means unanimous. The method consists of introducing a local analgesic solution, such as metycaine, into the peri-dural space *via* the sacral hiatus. One of the complications of this technique has been the breakage of needles, a difficulty which has now been overcome by the expedient of using a large needle, passing a catheter through it and then withdrawing the needle (Hingson and Edwards, 1942).

Those desiring to use this method would be well advised first to witness an actual demonstration by an experienced exponent of the technique. In the present state of knowledge and experience I hesitate to recommend it for routine employment, and venture to express the opinion that its possibilities should be the subject of further investigation.

ANÆSTHESIA FOR INSTRUMENTATION

Although some authorities prefer spinal analgesia for forceps delivery, the usual practice is to employ inhalation anæsthesia. Nitrous oxide, oxygen and cyclopropane will accomplish this with a freedom from toxicity and of after-effects, such as nausea and vomiting. A convenient alternative is nitrous oxide and ether in a portable apparatus, such as the McKesson, the Portanest, or Elam's modification of Boyle's apparatus.

EXTRA-UTERINE VERSION OF THE FŒTUS

The requirements are an adequate relaxation of the musculature of the abdominal wall and an absence of toxic effects. Premedication with atropine, 1/100 of a grain (0.65 mgm.), or scopolamine, 1/150 of a grain (0.43 mgm.), induction with nitrous oxide, and maintenance with cyclopropane, nitrous oxide and oxygen in closed circuit will usually suffice. If this does not afford sufficient relaxation it is better to add an adjuvant, such as vinesthene or ether, rather than to extend the depth of cyclopropane to near respiratory arrest. An alternative is nitrous oxide, oxygen and vinesthene, or ether in a

to secure anæsthesia for the last stages with this machine, but if used by an anæsthetist this may easily be accomplished by adding a Rowbotham's bottle containing an adjuvant, such as trilene, ether or vinesthene. When used by a midwife, the chief clinical difficulty is to secure a sufficiently quick action of the gas and air mixture to abolish discomfort during a labour pain. Experienced midwives overcome this by applying the face-piece in advance of the onset of a pain, and under guidance the average patient soon learns to cooperate intelligently.

In this country Moir and Elam have perfected means for enabling pure nitrous oxide gas to be inhaled at the onset of a pain, this being followed by the usual gas and air mixture. This is a valuable innovation and undoubtedly extends the scope of the gas and air method.

Trichlorethylene (*trilene*).—This is a quick-acting and effective analgesic drug which is non-inflammable, and for this reason is a valuable alternative agent to chloroform in domiciliary practice. Trilene vapour is non-irritant, easily breathed, and is not contraindicated in affections of the respiratory system.

Marrett has designed a useful apparatus which enables air to be drawn over trilene and permits a limited degree of re-breathing. With this apparatus, analgesia is easily and speedily produced and may be deepened into anæsthesia at the end of the second stage. The apparatus is portable, economic in use, and may be purchased at a reasonable price; advantages which render it suitable for use in general practice.

Freedman's bottle is an excellent device for self-administered analgesia with trilene (0.65 per cent.) and air. To bring the apparatus into action the patient breathes into the face-piece after covering an air hole with her finger, a precaution thus being provided against any loss of consciousness.

The technique for using trilene analgesia in labour is similar to that used with the gas and air machine, and is, in the opinion of many observers, a suitable alternative. The disadvantages of trilene are the occasional occurrence of tachypnœa, intermittent heart beat, and a cumulative action causing lack of cooperation. At the present time an investigation of trilene analgesia is being carried out by the Royal College of Obstetricians and Gynæcologists on the same lines as their investigation on chloroform and gas and air which yielded such valuable results some years ago.

Chloroform.—This drug is still used extensively by general practitioners in domiciliary practice. It has four advantages: speedy and efficient action; economy; non-inflammability; and simplicity of administration. Its disadvantages are:—

(a) Toxic effects on mother and fœtus.

(b) Tendency to prolong labour and cause uterine inertia with its sequelæ of increased need for instrumentation and post-partum hæmorrhage.

(c) Immediate clinical symptoms of an untoward or possibly fatal character.

ACNE VULGARIS AND ITS TREATMENT

By G. B. MITCHELL-HEGGS, O.B.E., M.D., F.R.C.P.

Physician in charge of Skin Department, St. Mary's Hospital; Physician, St. John's Hospital for Diseases of the Skin.

THE treatment of acne in general practice involves a review of the patient's general health and mode of life with correction of pathological conditions and alteration of habits when·indicated. In addition, there is the local treatment of the skin followed by the recognition in certain cases of intractability requiring specialist consideration and treatment.

PATHOGENESIS

The patient is usually young, between fifteen and twenty-five years of age, and the skin eruption is confined to the face, chest and back. Acne usually develops on a skin which is greyish white in colour, greasy and stippled by large sweat and sebaceous gland orifices. On palpation, a thickening, with deep-seated papules ranging from lentil to pea size, can be felt. These papules may be raised above the surface and are red and tender. Blackheads and pustules will be present, even in treated cases. The scalp is usually scurfy, especially near the temples, around the ears and near the vertex.

The cause of acne is indefinite, but in my opinion it is the summation of a number of factors. At puberty there is an increase in the activity of the skin, with an increase in the rate of growth of hair, and increase in the production of sebum. These factors are associated with the development of bran-like scales on the scalp. A greasy skin and scurfy head is a favourable habitat for the pityrosporon of Malassez, the acne bacillus and staphylococci. The orifices of the pilosebaceous follicles are often narrow and the opening occluded by a plug of sebaceous material. The sebaceous plug is almost always infected by these organisms, resulting in a surrounding inflammatory change. The nature of the infection, its virulence and the resulting inflammatory reaction lead to clinical signs in the form of simple blackheads, papules, pustules, larger tender cysts, and inflammatory thickening of the skin. Prolonged infection results in a diffuse low-grade inflammation with later pitting and scarring of the skin. Delay in the establishment of the normal endocrine and sex gland balance is a factor in many cases. Acne occurs in so many boys and girls that it can be described as physiological in origin, but when persistent or severe it is pathological and needs treatment. Severe cases are more common among boys than girls. The condition runs in certain families, especially those in which the males tend to go bald early. The tendency to the eruption remains from puberty to the menopause, but only a few patients are infected in the second half of the reproductive period. It is usually less severe in residents near the seaside or in the summer, but may be severe or aggravated by tropical heat. The logical treatment is to attempt to rectify the factors which can be

Boyle's machine. If an apparatus is not available, induction with ethyl chloride followed by open ether is the best substitute.

CÆSAREAN SECTION

The requirements are:—

   (1) Adequate relaxation.
   (2) No impairment of uterine retraction.
   (3) No respiratory depression of the fœtus.
   (4) No toxic effects.

Three methods are available:—

(1) *Inhalation anæsthesia* with nitrous oxide, oxygen and cyclopropane in a closed circuit apparatus. As an alternative, nitrous oxide, oxygen and minimal ether or vinesthene may be used in a Boyle's or other suitable machine. Premedication should be limited to atropine, 1/100 of a grain (0.65 mgm.).

(2) *Local analgesia* accomplishes all requirements satisfactorily, but the technique takes time and does not always suit the psychology of the patient. Over-dosage of local analgesics or undue sensitivity to their action may cause untoward symptoms.

(3) *Spinal analgesia.*—This is often satisfactory and fulfils all the requirements, but occasionally, from causes not fully understood, its use is associated with sudden collapse which may be fatal.

At the present time the inhalation method is most commonly used and may be safely recommended for the average case.

References

Cole, W. C. C. (1939): *Surg. Gynec. Obst.*, **68**, 179.
Hewer, C. Langton (1944): "Recent Advances in Anæsthesia and Analgesia," 5th edition, London, pp. 285, 291, 292.
Hingson, R. A., and Edwards, W. B. (1942): *Cur. Res. Anæs. Analg.*, **21**, 301.
Minnitt, R. G. (1944): "Gas and Air Analgesia", 2nd edition, London, p. 25.
Lloyd-Williams, K. G. (1941): Goldman's "Aids to Anæsthesia", London, p 161.

improvement has followed, but having seen a number of treated cases with enlargement of the male breast and a mild anxiety state, and others with no improvement in the acne, I do not recommend this line of therapy for males during the present state of knowledge of this branch of endocrinology. In resistant cases, however, stillbœstrol by mouth, in dosage of 1 mgm. twice daily for a period of four to six weeks, is reasonable and often successful.

Local therapy.—Scurf on the scalp is best removed in severe cases by gentle inunction of the skin at the hair roots with

℞ Precipitated sulphur   ..   20 grains (1.3 gm.) ⎫
   Salicylic acid..   ..   ..   5 grains (0.32 gm.) ⎪
   Soft soap *or*   ¼ ounce (3.9 gm.) ⎬ For dry scalps
   Halden's emulsifying base *simplex or*   ⎪
   Eucerin   ..   ..   to 1 ounce (28.4 gm.) ⎭

℞ Salicylic acid..   ..   ..   10 grains (0.65 gm.) ⎫
   Mercuric chloride   ..   ..   ¼ grain (0.016 gm.) ⎪
   Castor oil   ..   ..   5 minims (0.3 c.cm.) ⎬ for greasy heads
   Oil of rose geranium   ..   5 minims (0.3 c.cm.) ⎪
   Industrial spirit   ..   to 1 ounce (28.4 c.cm.) ⎭

every night for three nights, and a soap and water shampoo on the fourth night. This is practicable for men but must be adjusted for women to the days preceding their shampoo. Thorough rinsing is important.

The following treatment by the patient every evening is recommended:—

A clean hand towel is folded lengthwise and is placed in a saucepan of warm water so that 6 inches either end are not immersed; the water is then raised to boiling point, the towel lifted out, rung well and then brought near to the face; after about a minute's steaming it can usually be placed on the skin and then wrapped around the face. This hot pack is left on for ten to fifteen minutes. The moist greasy face is then well washed with soap and water and gently rubbed all over with the dry clean ends of the towel.

After three minutes one of the following lotions may be applied:—

℞ Zinc sulphate ..   ..   2 grains (0.13 gm.)
   Compound spirit of lavender   ..   ..   20 minims (1.2 c.cm.)
   Water ..   ..   to 1 ounce (28.4 c.cm.)

℞ Zinc sulphate ..   ..   10 grains (0.65 gm.)
   Sulphurated potash   ..   ..   ..   10 grains (0.65 gm.)
   Water ..   ..   to 1 ounce (28.4 c.cm.)

The proportion of sulphurated potash can be increased up to 60 grains (4 gm.) if the skin does not tend to become dry; if too drying, however, it can be made less so by decreasing the quantity of both and the addition of glycerin, 10 to 30 minims (0.6 c.cm. to 1.8 c.cm.). Useful alternatives are :—

℞ Resorcin   ..   ..   10 grains (0.65 gm.)
   Industrial spirit   ..   ..   ..   to 1 ounce (28.4 c.cm.)

or:—

℞ Precipitated sulphur ..   ..   10 grains (0.65 gm.)
   Calamine lotion   ..   ..   ..   to 1 ounce (28.4 c.cm.)
   [The amount of sulphur can be gradually increased to 30 grains (2 gm.)]

With all these lotions, when an erythema or desquamation develops it is best to stop the application for three days and so give the skin a chance to

regarded as influential in the particular case. Therefore it is important to consider every aspect of the patient's health when planning the treatment.

TREATMENT

People suffering from acne are usually of sound health but occasionally underlying ill health or abnormality seems to aggravate the condition, such as maleruption of teeth, a septic focus, including a "grumbling appendix", or chronic intestinal stasis. Appropriate treatment has been followed by improvement. Sudden eruption of a small group of acneiform lesions on one cheek only, may be associated with apical infection of teeth in the underlying jaw. I am not satisfied as to the exact pathological process but know that treatment of such an offending abscess is often followed by success.

General measures.—Constipation should be avoided by the use of a tumblerful of warm water on awakening, a morning saline, a cold infusion of senna pods or vegetable laxative pills. In all cases, plenty of fluids should also be taken. The following preparations should be avoided:—Those containing phenolphthalein, which can produce skin eruptions; blood tonics, which may include iodides; cough medicines and linctuses containing iodides or sedatives, such as compound tincture of camphor, which may encourage constipation.

Acne is usually worse in the winter when fruit and salads are scarce, and is seen in people who are still producing teeth and bone; so I usually prescribe vitamin C and calcium with vitamin D. If there is mental depression I prescribe the following mixture, which improves the appetite and the appearance of the skin, and promotes a feeling of well-being:—

> R Triple syrup .. .. .. 60 minims (3.5 c.cm.)
> Arsenical solution.. .. .. 2 minims (0.12 c.cm.)
> Orange flower water .. .. to ½ ounce (15 gm.)
> Three times a day before food.

The arsenic should not be continued for more than six weeks as there is a danger of hyperkeratosis and other signs of arsenic toxicity developing.

Diet and digestion play a part. It is best for patients with acne to avoid fatty foods, especially chocolate and cheese, pork and pastry. Articles in the diet which make the skin of the neck flush and the face go red and sweaty should be taken with moderation, especially coffee, curry, condiments, highly seasoned foods and alcohol.

Hormone therapy.—Acne is often seen in lethargic, well-covered individuals who may have a mild degree of thyroid insufficiency. They will improve on dry thyroid extract, ½ a grain (32 mgm.) twice daily, the dose to be adjusted according to the pulse rate, weight and tendency to excitability.

In some girls, delayed establishment of regular normal menstruation is associated with acne, and improvement follows the administration of œstrogens, such as stillbœstrol by mouth, 1 mgm. twice daily, following menstruation. In some cases the lesions are worse before menstruation.

Severe acne in young men has been treated with certain œstrogens and

although a course of sulphathiazole has benefited several patients. Penicillin is of use when there is heavy infection with penicillin-sensitive staphylococci. Systemic and local penicillin therapy are best combined. Penicillin, 100,000 units twice daily, combined with aspiration of the pus or sebaceous material and replacement with a few minims of a solution of penicillin, 200 units to 1 c.cm., is highly satisfactory in cases with many cysts. Such a course of treatment must of course be used in combination with those general measures already outlined.

X-RAY THERAPY

X-ray treatment should be initiated if the skin is remaining greasy and regularly producing papules and cysts in considerable numbers; it is hardly justifiable for mild cases with only occasional papules. Severe forms of acne, such as acne necrotica, acne conglobata, or complications, such as cheloidal changes in the skin, are best referred to a dermatologist.

THE PSYCHOLOGICAL ASPECT

An important aspect of the treatment of acne is psychological. It is reasonable to tell a young girl of fifteen that the lesions are due to her age and that she will grow out of the trouble, but most unkind to say the same in progressive cases or to men and women over eighteen years of age. The eruption leads to an inferiority complex and if not improving is soon associated with an anxiety state.

SOME PREDISPOSING FACTORS

Acne is frequently irritated or aggravated by life in a humid hot climate. Onset after eighteen years of age or a distribution on the forearm or thigh is seen in certain occupations, particularly those in which there is a continual splashing or soaking of the skin in oil, paraffin, or exposure to heat, soot, tar products, and certain chemicals. If the age of onset is not within the limits mentioned it is particularly important to exclude papular and pustular halogen salt eruptions. Administration of bromides, iodides, or male sex hormones will produce acneiform lesions. Rubbing the predisposed area with liniment or wearing wool or flannel vests may encourage an eruption.

Auto-inoculation.—Acne-form eruptions occur, even in babies, after inunction with oils. It is important to remember that infection can be spread by the hands on a skin which is heavily infected with the acne bacillus and staphylococci and covered with natural or applied oils or greases: their use should be minimized in cosmetic routine.

CONCLUSION

Whatever method of treatment is adopted the patient should be warned that the beneficial results only become slowly apparent and that each part of the regime and treatment must be carried out regularly and conscientiously.

return to normal. In certain cases this can be accelerated by the application of a calamine lotion, especially of the collosol type. It is best to avoid creams, ointments and oil.

Mild cases of acne treated at home with hot packs and lotions are assisted by *ultra-violet light therapy*, in gradually increased suberythema doses. In severe cases with considerable blackhead formation and pustulation, better results are obtained by repeating erythema doses once in ten to fourteen days. This produces a uniform peeling and can be repeated three or four times with safety. Severe sunburn and subsequent sensitization to the sun, or dermatitis medicamentosa through over-treatment, must be avoided, especially in very fair people or those with a history, or family history, of allergic skin diseases.

Removal of blackheads and cysts.—A number of patients squeeze the papules and cysts, and others are so obsessed by the disease that they dig the blackheads or cysts out with the nails. Blackheads should not be removed in this way but by means of a proper expressor which applies uniform pressure around the opening of the pilosebaceous follicles. Cystic lesions are best incised at the lowest point to ensure full drainage. A very small blade, size three, or a von Græfe knife is the best. A wick of silkworm gut can be left in for twenty-four hours to assist drainage. This conservative operation is best done by the practitioner rather than by the patient or relative. It is important to use this procedure for the lesions which contain pent-up sebaceous material or pus and not for the more solid erythematous papules. It is usually possible to select the correct papulo-pustular lesions for incision by gentle pressure on two sides of the lesion and looking for a translucent yellow central zone. The patient should be warned against squeezing cysts or purulent lesions without a preceding puncture, as it would lead to a subcutaneous spread of sebaceous material or pus. The ensuing aseptic and septic inflammation will produce greater scarring.

VACCINES AND CHEMOTHERAPY

A bacterial invasion of the skin is present in acne; it is therefore reasonable to try and raise the patient's immunity by means of a vaccine. Autogenous vaccines are usually better than stock mixtures. Whilst it is true that many patients are not benefited there are a number who do improve after vaccine therapy. It must be borne in mind, however, that too large a dose of vaccine will precipitate a relapse. Those cases in which there is a heavy staphylococcal infection with yellow pustules and frequent boils are benefited by injections of collosol manganese, or intramuscular injections of manganese butyrate, starting with $\frac{1}{2}$ c.cm. twice weekly for two weeks, and then 1 c.cm. A few patients respond to the administration of tin or yeast, and massive doses of vitamin A and B are worth trying in resistant cases when there is considerable pustulation and associated furunculosis. Chemotherapy has but a limited value. The sulphonamide group produce little improvement,

in active work of an essential nature and hence their return to health is less advertised than in the case of a worker returning to his job, and is therefore less spectacular. Fourthly, the percentage of deaths is inevitably much higher and, lastly, the pathology is often multiple and the majority need hospitalization, at least in the early stages of treatment.

But although treatment of such folk may in the past have been unprofitable to the individual practitioner, hospital or institution, the lack of treatment and failure to restore as full rehabilitation as possible is to-day proving most unprofitable to the community and, unless the problem of a first-class care of the aged is solved and a full geriatric service set up, these untreated cases may well cripple the Health Services of the country for many years to come.

PRESENT-DAY EXPECTATION OF LIFE

It will not be amiss here to quote figures showing the increase in the expectation of life to-day compared with former years, and to compare the number of people of sixty years and over who were living at the beginning of the century with the numbers living to-day (table 1 and 2).

TABLE 1

EXPECTATION OF LIFE IN GREAT BRITAIN

Year	Men	Women
1891/1900	44·1	47·8
1901/1910	48·5	52·4
1942	61·7	67·4

TABLE 2

POPULATION OF MEN AND WOMEN AGED SIXTY YEARS AND OVER IN GREAT BRITAIN

Year	Men	Women	Total
1901	1,071,519	1,336,907	2,408,426
1939	2,511,200	3,197,400	5,708,600
1944	2,737,000	3,590,000	6,327,000

It will be seen that the gross figures between 1901 and 1944 have been multiplied roughly by 2.5, i.e., from approximately 2½ millions to 6¼ millions alive to-day.

The absolute number of sick and infirm in any age-group cannot be estimated, as patients are treated at home as well as in institutions of all kinds. It is reasonable, however, to suggest that at the latter end of life there is at the present time probably at least as high a percentage of sick as

GERIATRICS: A MEDICAL, SOCIAL AND ECONOMIC PROBLEM

By MARJORY W. WARREN, M.R.C.S., L.R.C.P.

Deputy Medical Director, West Middlesex County Hospital, Isleworth.

THE care of the aged has been practised by medical people and others since the days of Hippocrates but, unlike other branches of medicine, it has never captured popular interest or developed into a specialty. Hence little research has been done on the diseases of old age, and little advance has been made in the treatment of these conditions.

Compared with work on other medical subjects there is scanty literature in this country on the diseases of old age, and as yet no medical journal on the subject has appeared in Great Britain, although the *Journal of Gerontology* published its first volume in America in January 1946. One of the earliest works on old age was written in the 13th century by Roger Bacon, an English scientist, but this was not translated into English until late in the 17th century and it was not until 1724 that the first medical work on diseases of old age, "Medicina Geroconica" was written by Floyer. During the next two centuries few outstanding contributions were made in this or other countries, and although a number of small works, many written for both medical and lay readers, were published, the majority lack scientific details of an academic nature. It is interesting to quote the following paragraph from Seidel's monograph "Diseases of Old Age", written in 1890:—

"Mistakes are made daily in the treatment of the Aged and the normal mortality of advanced life is considerably increased as a result of the hitherto neglected study of the peculiarities of the senile organism".

This quotation gives pause to wonder how far medicine has progressed in the care of the elderly sick since it was written.

The term "geriatric"—care of the aged—which was first used by Nascher in America in 1909, has not so far been widely accepted in this country. There are certain advantages, however, in the adoption of the term, for it defines the care of the aged as a separate subject and differentiates this group of patients from the larger class of "chronic cases" which includes those from all age-groups.

The reasons for lack of interest in the medical care of the aged are not far to seek. First, many such patients are on pension or much reduced incomes and are not very remunerative. Secondly, owing to impaired hearing and/or impaired sight, and to the nature of many of the conditions attendant upon old age, the time taken in getting a history and the patience required in examining such a patient are immeasurably greater than is necessary in dealing with younger patients. Thirdly, many of the conditions from which old people suffer take much longer to ameliorate and "cures" are often unobtainable. The majority of these patients have ceased to be engaged

person who has entered a hospital for treatment and, responding slowly or receiving no rehabilitation, finds himself confined for ever. He may demand his discharge but cannot these days get anywhere without outside help, for shortage of housing accommodation prevents him from getting easy billets, and often financial conditions prevent him from taking a flat or house. And even if accommodation and finance are available, the infirm need home help and cannot therefore be regarded as entirely independent.

No socially minded or thinking person would condone such conditions, yet these exist in hundreds of instances to-day, and a large number of elderly sick will be found untreated in institutions and even in hospitals. The resulting loss of morale is the most serious change which ensues, and this results in physical and mental deterioration, the patient becoming more and more helpless, dependent and difficult to care for and nurse, and eventually quite impossible to rehabilitate even to partial independence. Thus, not only do the institutions for the chronic sick become full and overcrowded, but alas the medical beds in the general hospitals also become blocked by lack of outlet.

Such conditions existed twenty years ago and still exist to-day, as confirmed by those who have visited patients in their evacuated hospitals during the war and/or by those patients who have returned from long bedridden sojourns in such places. If these conditions continue during the coming twenty years, then indeed the problem will be almost insoluble, for the numbers will be so great. This then is not only an economic problem of great magnitude but also a social problem, for no civilized people could condemn those of its workers, thinkers, planners and organizers, when their work for humanity is done, to suffer as indeed they must, both physically and mentally, under such conditions. Surely these folk who have worked so long for the community deserve the best that the country can give.

During this century the Health Services, especially those concerned in preventive medicine, have done much to prolong life, and this would be unjustified without providing the proper care for diseases and infirmities of advancing years. For who would desire to survive "the heat and toil of the battle" of life, only to linger neglected and cast off when too feeble to continue working?

THE NEED FOR TRAINING IN GERIATRICS

At the present time it is all too common to hear that senior members of the profession are not interested in the case of the chronic elderly sick, and even many erudite physicians do not retain such cases under their care if they can get them moved elsewhere. Thus there is little teaching on such patients, and the young medical graduate emerges from the Medical School as ignorant of these conditions and what can be done for them as did his seniors years ago; and so the tradition is handed on. If this attitude prevails among medical men, what of the nurses and ancillary staff ? Surely it

previously, which gives an absolute figure to-day for those requiring treatment and/or institutional care two-and-a-half times greater than at the beginning of the century. If it be remembered, too, that adequate home help and house room is now less than previously, the numbers will probably be considerably higher. Conversely, there is a smaller number of younger folk from whom to recruit the services necessary to care for these people.

This state of affairs has been growing almost imperceptibly and has been aggravated considerably by war conditions, so that now at the beginning of the post-war era the problem is one which demands immediate and urgent attention.

THE INADEQUACY OF EXISTING GERIATRIC SERVICES

In the past, with no comprehensive geriatric service, most hospitals in a desire to have a quick turnover have tried to reduce to a minimum the numbers of admissions of chronic sick cases, and of these chronic sick less interest and attention have been given to the aged than to others, with the result that they have been lamentably neglected from a medical point of view.

Inevitably the largest number of such patients have found their way into municipal hospitals and in turn into the various institutions for the chronic sick, often ill-assorted "dumps" for patients, who are housed in large wards which are devoid of any signs of comfort or interest. Such wards are all too familiar to those who know them; although scrupulously clean and with highly polished floors, they have dark walls, high windows, no furniture, no flowers, no lockers and there is no evidence of personal properties. The beds are neatly made in perfect line with each other and invariably tidy, for such is the rule, and as the patients become more helpless and disinterested so they conform more closely to the rigid impersonal system. Frequently the staff is disinterested in the patients, and even those who are not, lack the equipment, access of specialist consultations, and ancillary services found in a general hospital. As a result, investigations are reduced to a minimum and treatment almost entirely to nursing care only. In such institutions there is generally no scientific classification of patients and little or no improvement is expected. Large numbers of patients have found their way to these refuges and have remained there for long periods of time, and in some cases for ever.

The elderly are the silent sufferers in the community, for no school officer inquires of their progress, and no works manager asks when they will be fit for discharge. Their relatives are too often pleased to be relieved of responsibility for them, and their friends, often of a contemporary age, have neither the physical nor mental energy to demand better attention and, whilst willing to visit as regularly and for as long as they are able, cannot do more, and silently hope that the time will not come when they too must enter such a place. Nobody is more truly imprisoned than an elderly infirm

psychological can be catered for. In order to do this under the best conditions, a specialized service for old people should be set up, and it is seriously suggested and strongly recommended that a Service of Geriatrics be recognized and given full status and encouragement, equal to other branches of medicine, such as pædiatrics. Under such conditions it is expected that more medical people will be found to undertake this work and that they will find it satisfying, interesting and profitable to the advancement of medicine and to the advantage of the community.

Such a geriatric service, well directed and under the leadership of medical staff with vision and energy, should include:—

(1) An acute geriatric unit as part of a general hospital.

(2) Long-stay annexes attached to a geriatric unit in a hospital.

(3) Resident homes for the reception of those aged who, having recovered from illness, are for any reason unable to return to their own home.'

Such a service should undertake:—

(1) To diagnose and treat the aged sick, under properly classified conditions.

(2) To be responsible for the teaching of medical students, student nurses and others in the diseases and care of the ageing.

(3) To initiate research in the diseases affecting old age.

(4) To supervise and advise in the care and welfare of the aged.

The *acute geriatric unit* in the general hospital should receive on admission *all* medical patients over sixty years of age and surgical patients of the same age who require investigation before operation. There are usually not sufficient surgical emergencies in this age-group to justify setting aside geriatric surgical wards. These latter patients should be transferred to surgical wards for operative treatment only, and should then return to the geriatric unit for convalescence and/or rehabilitation. Wards in the geriatric unit should be classified to deal with different types of conditions:—

(a) Wards equipped with cot beds, for restless patients and others who do not need to be treated as mental patients.

(b) Wards equipped for the investigation of incontinence and treatment, including re-education of such cases.

(c) Wards divided into small, probably four-bedded sections, for treatment of other medical conditions, allowing for segregation and privacy.

The *long-stay annexes* should only be used for patients who have been given the maximum opportunity of recovery in the acute geriatric unit, and who are ultimately found to be unable to benefit further from active medical treatment. These annexes, which may be within or without the hospital grounds according to convenience, should remain under the supervision of the medical staff of the geriatric department, and the patients, who should be watched for material change in condition, should be regularly visited by such medical staff. The services of dietitians, almoners, physiotherapists and occupational therapists are also essential.

would seem reasonable to select the most skilled and best nursing staff for such patients, because of the enfeebled physical and mental condition of many, frequently afflicted with more than one pathological condition or degeneration. Yet this is not so to-day. Still are student nurses guarded from training on such wards, and junior staff considered suitable to take charge. Still do many physiotherapists show preference for the orthopædic case in the younger groups because of the quicker, easier and more spectacular results to be obtained.

The result of this treatment of patients is disastrous in the majority of cases. Relegated to the care of disinterested and apathetic medical staff, in the absence of initiative and without the services of ancillary staff, large numbers remain in bed and become permanently bedridden, and the general physical and psychological deterioration which follows makes them very heavy cases to nurse and eventually quite uninteresting to look after, as no improvement can be expected.

It may not be out of place here to cite an example illustrating this point:—

In the summer of 1945, hospital A received a number of cases previously treated in hospital B, returning from an evacuated hospital C where they had been for over eleven months. These forty-two patients, of whom six only were under sixty years and twenty-nine were over seventy years, were all completely bedridden, doubly incontinent and helpless. The majority were disinterested in themselves, having lost faith in a future different from the present; all had disuse contractures and *all* were fed by nursing staff. Examination of their papers showed that all had been in bed for a minimum period of over fifteen months and some for over three years. The majority were patients with cerebral thrombosis, but there were others, including some with arthritis, myocardial degeneration and the results of accidents, e.g. fractured neck of femur and avulsion of anterior part of foot. No operations were performed but the regular care and treatment of these patients was instituted as soon as they arrived and with the help of a very cooperative ward sister and nursing and physiotherapist staff, who were experienced in this type of work, a small number were rescued from their hopeless condition and the following results were obtained:—In three months five patients or 12 per cent. were up and about and discharged, another three patients or 7 per cent. were walking a little with assistance, seventeen others or 40 per cent. were out of bed sitting in chairs part or all day, and *all* were feeding themselves.

This experience, by no means unique, suggests that one of the first things necessary is for all medical staff at present taking care of the so-called "chronic sick" to examine their patients afresh in the light of these facts, in order to find out how many could be improved, either sufficiently to go home or to be transferred to a resident home, where they would lead more interesting lives and be cared for more economically; or, failing this, how many patients could be made less dependent in the matter of caring for their needs, e.g. feeding and the like.

FUTURE NEEDS

In making plans for the future it seems advisable from every point of view to provide for these elderly folk, apart from those in the younger age-groups and apart from children, so that their special needs both physical and

psychological can be catered for. In order to do this under the best conditions, a specialized service for old people should be set up, and it is seriously suggested and strongly recommended that a Service of Geriatrics be recognized and given full status and encouragement, equal to other branches of medicine, such as pædiatrics. Under such conditions it is expected that more medical people will be found to undertake this work and that they will find it satisfying, interesting and profitable to the advancement of medicine and to the advantage of the community.

Such a geriatric service, well directed and under the leadership of medical staff with vision and energy, should include:—

(1) An acute geriatric unit as part of a general hospital.

(2) Long-stay annexes attached to a geriatric unit in a hospital.

(3) Resident homes for the reception of those aged who, having recovered from illness, are for any reason unable to return to their own home.

Such a service should undertake:—

(1) To diagnose and treat the aged sick, under properly classified conditions.

(2) To be responsible for the teaching of medical students, student nurses and others in the diseases and care of the ageing.

(3) To initiate research in the diseases affecting old age.

(4) To supervise and advise in the care and welfare of the aged.

The *acute geriatric unit* in the general hospital should receive on admission *all* medical patients over sixty years of age and surgical patients of the same age who require investigation before operation. There are usually not sufficient surgical emergencies in this age-group to justify setting aside geriatric surgical wards. These latter patients should be transferred to surgical wards for operative treatment only, and should then return to the geriatric unit for convalescence and/or rehabilitation. Wards in the geriatric unit should be classified to deal with different types of conditions:—

(a) Wards equipped with cot beds, for restless patients and others who do not need to be treated as mental patients.

(b) Wards equipped for the investigation of incontinence and treatment, including re-education of such cases.

(c) Wards divided into small, probably four-bedded sections, for treatment of other medical conditions, allowing for segregation and privacy.

The *long-stay annexes* should only be used for patients who have been given the maximum opportunity of recovery in the acute geriatric unit, and who are ultimately found to be unable to benefit further from active medical treatment. These annexes, which may be within or without the hospital grounds according to convenience, should remain under the supervision of the medical staff of the geriatric department, and the patients, who should be watched for material change in condition, should be regularly visited by such medical staff. The services of dietitians, almoners, physiotherapists and occupational therapists are also essential.

Sodium citrate only had the effect of making the curds slightly smaller. At feeding times, which were necessarily frequent, the child would start suckling avidly but almost immediately lapse into a semi-comatose state, with extreme pallor, shallow respiration, raised pulse, and complete flaccidity. Taken as evidence of vasomotor instability, thiamine hydrochloride $1\frac{1}{2}$ mgm. orally, three times a day, was given to the baby, with no effect.

As time passed, the syncopal attacks became less severe, but were still regular. Owing to the mother's condition and loss of weight in the child, supplementary feeding was begun and the child's general condition improved slightly, the stools now becoming pale, fatty and bulkier, with smaller particles of casein.

A month after confinement the mother developed abscesses in the right axilla which persisted intermittently for three weeks, redness and induration remaining in between periods of suppuration, in spite of local applications and sulphonamide therapy. An iron and arsenic mixture was then tried with no apparent effect, but while still taking this mixture the mother was given acetomenaphthone with the object of improving the baby's fat digestion. Within three days the axillary condition was practically healed, swelling and tenderness had almost disappeared, and the patient stated that she felt much better. Her appearance changed completely within a week; the bowels became regular, appetite increased and she seemed full of energy and did not complain of any feeling of fatigue.

The child began to gain in weight, became lively and was able to stay awake to take full feeds. Her stools became smaller in bulk but still pale and fatty, although the caseinous masses disappeared. Riboflavin was then given to the mother twice daily in addition to the acetomenaphthone and the child's stools promptly became yellow and of normal bulk. On each of four occasions when acetomenaphthone was withdrawn symptoms of both mother and child returned within five days of each withdrawal.

After five-and-a-half months the mother is still taking vitamin K analogue and riboflavin twice daily, and is very well. The child is progressing normally, is happy and contented but refuses to relinquish her occasional breast feed.

CASE 2.—C.W., aged twenty, had a history of infantile eczema at the age of nine months, lasting until she was two years old, when she began to suffer from attacks of asthma. These were frequent and troublesome, often calling for the use of adrenaline or ephedrine. From the onset, at the age of fifteen, menstruation had been irregular, with long periods of amenorrhœa, during which attacks of asthma were more frequent and severe. At the age of seventeen she was confined to bed for three months with intractable asthmatic bronchitis, hæmoptysis and loss of weight. On examination there was no trace, clinically or radiologically, of tuberculous or other fibrosis. Carious teeth were subsequently removed and attacks ceased for a few months. After further recurrences, relieved for shorter or longer periods by further dental extractions, an anti-catarrhal vaccine was given six months ago with great improvement in general health and for two months freedom from attacks.

For the next two months attacks recurred, with frequency increasing to two attacks weekly, each lasting for two to three days. She was then given acetomenaphthone, 10 mgm. daily, and nicotinic acid, 50 mgm. twice daily. After three days the patient was free of symptoms and remained so for seven weeks with one six-hour attack when supplies of the vitamin failed. Menstruation is now regular and full, the patient leads a very active life and she states that she has never felt so well in her life.

CASE 3.—M.E., aged eight-and-a-half years, suffering from chronic nasal catarrh, has from birth been unusually susceptible to "colds and chills", a cold wind or wetting the head or feet being sufficient to precipitate an attack of acute asthmatic bronchitis. At the best of times he suffered from nocturnal wheeziness and noisy mouth-breathing. Appetite and activity were normal.

Vaccines having failed to bring about any improvement he was given acetomenaphthone, 10 mgm. daily, and nicotinic acid, 50 mgm. night and morning. There was marked improvement in the nasal condition, breathing becoming normal at night with cessation of the wheezy cough. For a week the child did most of the

things which would formerly have promptly resulted in an acute attack of bronchitis and asthma. On cessation of the treatment slight wheeziness and noisy breathing returned within three days.

CASE 4.—B.W., aged fifteen, fell and hurt her left knee slightly on April 4, 1946. There was no apparent injury. On April 11 she could not bend the knee. There was swelling and redness in the infrapatellar region, with acute tenderness.

She was given acetomenaphthone, 10 mgm. twice daily, and hot foments were applied to the knee. On the next day cellulitis had spread downwards to midway between the knee and ankle and the temperature rose to 101° F. (38.3° C.). On the following day the temperature dropped to normal and the swelling disappeared rapidly leaving only a faint bluish discoloration of the skin.

April 14: There was no trace of any inflammatory process having taken place, apart from slight stiffness on walking.

CASE 5.—B.G.R., aged ten, had sores and scabs over the whole of the scalp for twelve months. Lotions, tonic medicines, sulphonamides, internally and externally, and penicillin had been tried with no avail. The child was pale, tired-looking, irritable, restless at night and had no appetite for play or food.

On April 8 she was given acetomenaphthone, 10 mgm. daily, nicotinic acid, 50 mgm. twice daily, and an iron and arsenic mixture, the head being kept dry with talcum powder.

April 15 : More than half the scabs were loose and inflammation surrounding the remainder had practically disappeared. The child looked well and happy and her mother expressed amazement at the improvement in the child's general condition. Dilute ammoniated mercury ointment was given to be applied to the remaining scabs.

April 22 : Head practically clear.

May 6 : No trace of original condition and child is in perfect health.

DISCUSSION

Many other similar cases have been treated, including primary colds, chills, acute nasal catarrh, acute sinusitis, acute catarrhal bronchitis, influenza, and chronic tonsillar and dental sepsis.

I have also observed that in patients requiring morphine or its derivatives while being treated with acetomenaphthone, the expected nausea and malaise were absent.

The diversity of conditions which seem susceptible to treatment with vitamin K suggests that this vitamin may have some importance in the mechanism of resistance to infection, possibly by facilitating detoxication. As prothrombin, an essential factor in the defence of the body, is synthesized by the liver with the aid of vitamin K, and since the liver, the chief detoxicating centre of the body, is responsible, by virtue of its secretion of bile salts, for the absorption of this vitamin, it seems likely that vitamin K might also be essential to the liver in that other phase of defence, namely, detoxication.

In conclusion, I do not suggest that vitamin K or its analogue can be used with safety in each and every case of toxæmia, but my experiences, of which I have described a few examples, have led me to believe that further investigation and trial of vitamin K in this connexion would be justifiable and, I believe, would bring to light a valuable aid in the field of therapeutics.

Sodium citrate only had the effect of making the curds slightly smaller. At feeding times, which were necessarily frequent, the child would start suckling avidly but almost immediately lapse into a semi-comatose state, with extreme pallor, shallow respiration, raised pulse, and complete flaccidity. Taken as evidence of vasomotor instability, thiamine hydrochloride 1½ mgm. orally, three times a day, was given to the baby, with no effect.

As time passed, the syncopal attacks became less severe, but were still regular. Owing to the mother's condition and loss of weight in the child, supplementary feeding was begun and the child's general condition improved slightly, the stools now becoming pale, fatty and bulkier, with smaller particles of casein.

A month after confinement the mother developed abscesses in the right axilla which persisted intermittently for three weeks, redness and induration remaining in between periods of suppuration, in spite of local applications and sulphonamide therapy. An iron and arsenic mixture was then tried with no apparent effect, but while still taking this mixture the mother was given acetomenaphthone with the object of improving the baby's fat digestion. Within three days the axillary condition was practically healed, swelling and tenderness had almost disappeared, and the patient stated that she felt much better. Her appearance changed completely within a week; the bowels became regular, appetite increased and she seemed full of energy and did not complain of any feeling of fatigue.

The child began to gain in weight, became lively and was able to stay awake to take full feeds. Her stools became smaller in bulk but still pale and fatty, although the caseinous masses disappeared. Riboflavin was then given to the mother twice daily in addition to the acetomenaphthone and the child's stools promptly became yellow and of normal bulk. On each of four occasions when acetomenaphthone was withdrawn symptoms of both mother and child returned within five days of each withdrawal.

After five-and-a-half months the mother is still taking vitamin K analogue and riboflavin twice daily, and is very well. The child is progressing normally, is happy and contented but refuses to relinquish her occasional breast feed.

CASE 2.—C.W., aged twenty, had a history of infantile eczema at the age of nine months, lasting until she was two years old, when she began to suffer from attacks of asthma. These were frequent and troublesome, often calling for the use of adrenaline or ephedrine. From the onset, at the age of fifteen, menstruation had been irregular, with long periods of amenorrhœa, during which attacks of asthma were more frequent and severe. At the age of seventeen she was confined to bed for three months with intractable asthmatic bronchitis, hæmoptysis and loss of weight. On examination there was no trace, clinically or radiologically, of tuberculous or other fibrosis. Carious teeth were subsequently removed and attacks ceased for a few months. After further recurrences, relieved for shorter or longer periods by further dental extractions, an anti-catarrhal vaccine was given six months ago with great improvement in general health and for two months freedom from attacks.

For the next two months attacks recurred, with frequency increasing to two attacks weekly, each lasting for two to three days. She was then given acetomenaphthone, 10 mgm. daily, and nicotinic acid, 50 mgm. twice daily. After three days the patient was free of symptoms and remained so for seven weeks with one six-hour attack when supplies of the vitamin failed. Menstruation is now regular and full, the patient leads a very active life and she states that she has never felt so well in her life.

CASE 3.—M.E., aged eight-and-a-half years, suffering from chronic nasal catarrh, has from birth been unusually susceptible to "colds and chills", a cold wind or wetting the head or feet being sufficient to precipitate an attack of acute asthmatic bronchitis. At the best of times he suffered from nocturnal wheeziness and noisy mouth-breathing. Appetite and activity were normal.

Vaccines having failed to bring about any improvement he was given acetomenaphthone, 10 mgm. daily, and nicotinic acid, 50 mgm. night and morning. There was marked improvement in the nasal condition, breathing becoming normal at night with cessation of the wheezy cough. For a week the child did most of the

things which would formerly have promptly resulted in an acute attack of bronchitis and asthma. On cessation of the treatment slight wheeziness and noisy breathing returned within three days.

CASE 4.—B.W., aged fifteen, fell and hurt her left knee slightly on April 4, 1946. There was no apparent injury. On April 11 she could not bend the knee. There was swelling and redness in the infrapatellar region, with acute tenderness.

She was given acetomenaphthone, 10 mgm. twice daily, and hot foments were applied to the knee. On the next day cellulitis had spread downwards to midway between the knee and ankle and the temperature rose to 101° F. (38.3° C.). On the following day the temperature dropped to normal and the swelling disappeared rapidly leaving only a faint bluish discoloration of the skin.

April 14: There was no trace of any inflammatory process having taken place, apart from slight stiffness on walking.

CASE 5.—B.G.R., aged ten, had sores and scabs over the whole of the scalp for twelve months. Lotions, tonic medicines, sulphonamides, internally and externally, and penicillin had been tried with no avail. The child was pale, tired-looking, irritable, restless at night and had no appetite for play or food.

On April 8 she was given acetomenaphthone, 10 mgm. daily, nicotinic acid, 50 mgm. twice daily, and an iron and arsenic mixture, the head being kept dry with talcum powder.

April 15 : More than half the scabs were loose and inflammation surrounding the remainder had practically disappeared. The child looked well and happy and her mother expressed amazement at the improvement in the child's general condition. Dilute ammoniated mercury ointment was given to be applied to the remaining scabs.

April 22 : Head practically clear.

May 6 : No trace of original condition and child is in perfect health.

DISCUSSION

Many other similar cases have been treated, including primary colds, chills, acute nasal catarrh, acute sinusitis, acute catarrhal bronchitis, influenza, and chronic tonsillar and dental sepsis.

I have also observed that in patients requiring morphine or its derivatives while being treated with acetomenaphthone, the expected nausea and malaise were absent.

The diversity of conditions which seem susceptible to treatment with vitamin K suggests that this vitamin may have some importance in the mechanism of resistance to infection, possibly by facilitating detoxication. As prothrombin, an essential factor in the defence of the body, is synthesized by the liver with the aid of vitamin K, and since the liver, the chief detoxicating centre of the body, is responsible, by virtue of its secretion of bile salts, for the absorption of this vitamin, it seems likely that vitamin K might also be essential to the liver in that other phase of defence, namely, detoxication.

In conclusion, I do not suggest that vitamin K or its analogue can be used with safety in each and every case of toxæmia, but my experiences, of which I have described a few examples, have led me to believe that further investigation and trial of vitamin K in this connexion would be justifiable and, I believe, would bring to light a valuable aid in the field of therapeutics.

THE EARLY RECOGNITION OF DISEASE
XI.—MALIGNANT DISEASE

By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

IT is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

confirm them. In the first place, knowledge of family histories may have a definite bearing on the problem. It is now admitted by statisticians that an inherited tendency to the formation of cancer does exist, that there are, in fact, "cancer strains" in men as well as in mice, and this may well influence a medical opinion, especially in relation to a diagnosis of *cancer of the breast*. The daughter of parents either of whom has had cancer in any form is slightly more liable to develop cancer of the breast than another individual whose family history is free of the tendency; but the daughter of a mother who has had cancer of the breast is much more likely to develop it herself than another, and due weight must be given to this increased liability in face of doubtful indications.

Again, it is well known that certain families show an extraordinary incidence of *cancer of the rectum or colon*, and that this is due to an inherited tendency to produce papillomas of the large bowel, which are at first innocent, but usually change, sooner or later, to malignant neoplasms. The implications of this are obvious, and even (perhaps particularly) the younger members of such a family must be kept under most careful supervision.

There is a widespread belief among the laity that cancer must be a consequence of ill health, and quite evident external lesions may thus be ignored because the victim is otherwise well. The trained medical observer is unlikely to be influenced by this fallacy, but he is sometimes guilty of ignoring the early signs of early *internal cancer* because they seem so trivial, and inevitably it will always be a matter of the greatest difficulty to decide when to begin investigations on account of trivial signs. Thus, one of the organs most commonly affected by cancer is the stomach, a fact which might be expected to lead to frequent early diagnosis with good hope of cure. Yet cancer of the stomach carries one of the lowest curability rates of all: a discouraging fact for those who think that familiarity with the signs of disease should make diagnosis easier. It is, indeed, necessary to think along lines of prevention rather than of "cure" in the effort to decrease the mortality from the various forms of internal cancer. Prevention, however, at once necessitates a fuller and more accurate knowledge of the causes of cancer than at present available, so that again discouragement is felt.

THE NASOPHARYNX AND ALIMENTARY TRACT

It may be instructive to consider briefly the possible early indications, or the lack of them, in malignant disease of the nasopharynx and alimentary tract. To begin with a commonly affected sinus, the maxillary antrum, it is true to say that the early stages of a carcinoma in this enclosed space cause symptoms so slight that early diagnosis is virtually impossible. A slight unilateral catarrh is unlikely to bring a patient to his doctor, and by the time there is obstruction, or pain, or a blood-stained discharge the disease is no longer early. The best hope is that any noticeable discharge may soon become purulent or offensive; features which are more likely to lead to

THE EARLY RECOGNITION OF DISEASE
XI.—MALIGNANT DISEASE

By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

IT is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

confirm them. In the first place, knowledge of family histories may have a definite bearing on the problem. It is now admitted by statisticians that an inherited tendency to the formation of cancer does exist, that there are, in fact, "cancer strains" in men as well as in mice, and this may well influence a medical opinion, especially in relation to a diagnosis of *cancer of the breast*. The daughter of parents either of whom has had cancer in any form is slightly more liable to develop cancer of the breast than another individual whose family history is free of the tendency; but the daughter of a mother who has had cancer of the breast is much more likely to develop it herself than another, and due weight must be given to this increased liability in face of doubtful indications.

Again, it is well known that certain families show an extraordinary incidence of *cancer of the rectum or colon*, and that this is due to an inherited tendency to produce papillomas of the large bowel, which are at first innocent, but usually change, sooner or later, to malignant neoplasms. The implications of this are obvious, and even (perhaps particularly) the younger members of such a family must be kept under most careful supervision.

There is a widespread belief among the laity that cancer must be a consequence of ill health, and quite evident external lesions may thus be ignored because the victim is otherwise well. The trained medical observer is unlikely to be influenced by this fallacy, but he is sometimes guilty of ignoring the early signs of early *internal cancer* because they seem so trivial, and inevitably it will always be a matter of the greatest difficulty to decide when to begin investigations on account of trivial signs. Thus, one of the organs most commonly affected by cancer is the stomach, a fact which might be expected to lead to frequent early diagnosis with good hope of cure. Yet cancer of the stomach carries one of the lowest curability rates of all: a discouraging fact for those who think that familiarity with the signs of disease should make diagnosis easier. It is, indeed, necessary to think along lines of prevention rather than of "cure" in the effort to decrease the mortality from the various forms of internal cancer. Prevention, however, at once necessitates a fuller and more accurate knowledge of the causes of cancer than at present available, so that again discouragement is felt.

THE NASOPHARYNX AND ALIMENTARY TRACT

It may be instructive to consider briefly the possible early indications, or the lack of them, in malignant disease of the nasopharynx and alimentary tract. To begin with a commonly affected sinus, the maxillary antrum, it is true to say that the early stages of a carcinoma in this enclosed space cause symptoms so slight that early diagnosis is virtually impossible. A slight unilateral catarrh is unlikely to bring a patient to his doctor, and by the time there is obstruction, or pain, or a blood-stained discharge the disease is no longer early. The best hope is that any noticeable discharge may soon become purulent or offensive; features which are more likely to lead to

THE EARLY RECOGNITION OF DISEASE

XI.—MALIGNANT DISEASE

By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

IT is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

confirm them. In the first place, knowledge of family histories may have a definite bearing on the problem. It is now admitted by statisticians that an inherited tendency to the formation of cancer does exist, that there are, in fact, "cancer strains" in men as well as in mice, and this may well influence a medical opinion, especially in relation to a diagnosis of *cancer of the breast*. The daughter of parents either of whom has had cancer in any form is slightly more liable to develop cancer of the breast than another individual whose family history is free of the tendency; but the daughter of a mother who has had cancer of the breast is much more likely to develop it herself than another, and due weight must be given to this increased liability in face of doubtful indications.

Again, it is well known that certain families show an extraordinary incidence of *cancer of the rectum or colon*, and that this is due to an inherited tendency to produce papillomas of the large bowel, which are at first innocent, but usually change, sooner or later, to malignant neoplasms. The implications of this are obvious, and even (perhaps particularly) the younger members of such a family must be kept under most careful supervision.

There is a widespread belief among the laity that cancer must be a consequence of ill health, and quite evident external lesions may thus be ignored because the victim is otherwise well. The trained medical observer is unlikely to be influenced by this fallacy, but he is sometimes guilty of ignoring the early signs of early *internal cancer* because they seem so trivial, and inevitably it will always be a matter of the greatest difficulty to decide when to begin investigations on account of trivial signs. Thus, one of the organs most commonly affected by cancer is the stomach, a fact which might be expected to lead to frequent early diagnosis with good hope of cure. Yet cancer of the stomach carries one of the lowest curability rates of all: a discouraging fact for those who think that familiarity with the signs of disease should make diagnosis easier. It is, indeed, necessary to think along lines of prevention rather than of "cure" in the effort to decrease the mortality from the various forms of internal cancer. Prevention, however, at once necessitates a fuller and more accurate knowledge of the causes of cancer than at present available, so that again discouragement is felt.

THE NASOPHARYNX AND ALIMENTARY TRACT

It may be instructive to consider briefly the possible early indications, or the lack of them, in malignant disease of the nasopharynx and alimentary tract. To begin with a commonly affected sinus, the maxillary antrum, it is true to say that the early stages of a carcinoma in this enclosed space cause symptoms so slight that early diagnosis is virtually impossible. A slight unilateral catarrh is unlikely to bring a patient to his doctor, and by the time there is obstruction, or pain, or a blood-stained discharge the disease is no longer early. The best hope is that any noticeable discharge may soon become purulent or offensive; features which are more likely to lead to

THE EARLY RECOGNITION OF DISEASE
XI.—MALIGNANT DISEASE
By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

It is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

confirm them. In the first place, knowledge of family histories may have a definite bearing on the problem. It is now admitted by statisticians that an inherited tendency to the formation of cancer does exist, that there are, in fact, "cancer strains" in men as well as in mice, and this may well influence a medical opinion, especially in relation to a diagnosis of *cancer of the breast*. The daughter of parents either of whom has had cancer in any form is slightly more liable to develop cancer of the breast than another individual whose family history is free of the tendency; but the daughter of a mother who has had cancer of the breast is much more likely to develop it herself than another, and due weight must be given to this increased liability in face of doubtful indications.

Again, it is well known that certain families show an extraordinary incidence of *cancer of the rectum or colon,* and that this is due to an inherited tendency to produce papillomas of the large bowel, which are at first innocent, but usually change, sooner or later, to malignant neoplasms. The implications of this are obvious, and even (perhaps particularly) the younger members of such a family must be kept under most careful supervision.

There is a widespread belief among the laity that cancer must be a consequence of ill health, and quite evident external lesions may thus be ignored because the victim is otherwise well. The trained medical observer is unlikely to be influenced by this fallacy, but he is sometimes guilty of ignoring the early signs of early *internal cancer* because they seem so trivial, and inevitably it will always be a matter of the greatest difficulty to decide when to begin investigations on account of trivial signs. Thus, one of the organs most commonly affected by cancer is the stomach, a fact which might be expected to lead to frequent early diagnosis with good hope of cure. Yet cancer of the stomach carries one of the lowest curability rates of all: a discouraging fact for those who think that familiarity with the signs of disease should make diagnosis easier. It is, indeed, necessary to think along lines of prevention rather than of "cure" in the effort to decrease the mortality from the various forms of internal cancer. Prevention, however, at once necessitates a fuller and more accurate knowledge of the causes of cancer than at present available, so that again discouragement is felt.

THE NASOPHARYNX AND ALIMENTARY TRACT

It may be instructive to consider briefly the possible early indications, or the lack of them, in malignant disease of the nasopharynx and alimentary tract. To begin with a commonly affected sinus, the maxillary antrum, it is true to say that the early stages of a carcinoma in this enclosed space cause symptoms so slight that early diagnosis is virtually impossible. A slight unilateral catarrh is unlikely to bring a patient to his doctor, and by the time there is obstruction, or pain, or a blood-stained discharge the disease is no longer early. The best hope is that any noticeable discharge may soon become purulent or offensive; features which are more likely to lead to

THE EARLY RECOGNITION OF DISEASE

XI.—MALIGNANT DISEASE

By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

IT is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

confirm them. In the first place, knowledge of family histories may have a definite bearing on the problem. It is now admitted by statisticians that an inherited tendency to the formation of cancer does exist, that there are, in fact, "cancer strains" in men as well as in mice, and this may well influence a medical opinion, especially in relation to a diagnosis of *cancer of the breast*. The daughter of parents either of whom has had cancer in any form is slightly more liable to develop cancer of the breast than another individual whose family history is free of the tendency; but the daughter of a mother who has had cancer of the breast is much more likely to develop it herself than another, and due weight must be given to this increased liability in face of doubtful indications.

Again, it is well known that certain families show an extraordinary incidence of *cancer of the rectum or colon*, and that this is due to an inherited tendency to produce papillomas of the large bowel, which are at first innocent, but usually change, sooner or later, to malignant neoplasms. The implications of this are obvious, and even (perhaps particularly) the younger members of such a family must be kept under most careful supervision.

There is a widespread belief among the laity that cancer must be a consequence of ill health, and quite evident external lesions may thus be ignored because the victim is otherwise well. The trained medical observer is unlikely to be influenced by this fallacy, but he is sometimes guilty of ignoring the early signs of early *internal cancer* because they seem so trivial, and inevitably it will always be a matter of the greatest difficulty to decide when to begin investigations on account of trivial signs. Thus, one of the organs most commonly affected by cancer is the stomach, a fact which might be expected to lead to frequent early diagnosis with good hope of cure. Yet cancer of the stomach carries one of the lowest curability rates of all: a discouraging fact for those who think that familiarity with the signs of disease should make diagnosis easier. It is, indeed, necessary to think along lines of prevention rather than of "cure" in the effort to decrease the mortality from the various forms of internal cancer. Prevention, however, at once necessitates a fuller and more accurate knowledge of the causes of cancer than at present available, so that again discouragement is felt.

THE NASOPHARYNX AND ALIMENTARY TRACT

It may be instructive to consider briefly the possible early indications, or the lack of them, in malignant disease of the nasopharynx and alimentary tract. To begin with a commonly affected sinus, the maxillary antrum, it is true to say that the early stages of a carcinoma in this enclosed space cause symptoms so slight that early diagnosis is virtually impossible. A slight unilateral catarrh is unlikely to bring a patient to his doctor, and by the time there is obstruction, or pain, or a blood-stained discharge the disease is no longer early. The best hope is that any noticeable discharge may soon become purulent or offensive; features which are more likely to lead to

THE EARLY RECOGNITION OF DISEASE

XI.—MALIGNANT DISEASE

By GEOFFREY KEYNES, M.D., F.R.C.S.

Surgeon, St. Bartholomew's Hospital.

IT is everywhere admitted that in spite of intensive research into the cause and cure of malignant disease the most potent weapon against it remains in the realm of early diagnosis. Cancer is a curable disease in its early stages, and it is only the frequency of incurable disease resulting from delayed diagnosis that has given even the more educated sections of the people the idea that it is always hopeless. This has often resulted in concealment of disease by patients until concealment was no longer possible, and with disastrous results. Education of medical students has also been at fault, both teachers and textbooks having insisted on the diagnostic signs and symptoms of advanced disease, whilst remaining silent on the early signs and on the general attitude to be adopted by a medical man in face of doubtful signs which could arouse no more than suspicions in his mind. Sometimes, perhaps, a medical practitioner feels a delicacy and kindness towards his patients which makes him reluctant to suggest investigations, fearing that they may only arouse unnecessary mental distress. And so a wait-and-see policy is initiated which misses the golden opportunity of making an early diagnosis. Far better, however, to make a few mistakes on the right side than sacrifice a patient's life by default.

Much has been written about the danger of creating a cancer-conscious and hypochondriac population by publicizing "the facts about cancer". But the consciousness is already there in a misguided form. Every woman who discovers a lump in her breast believes that she has cancer, and most women who have pain in a breast have at least an uneasiness on the same score. Greater knowledge and more prompt investigation will serve to dissipate, rather than to increase, the phobias and inhibitions which surround the whole subject.

Yet when an attempt is made to assess the value of doubtful signs and early indications great difficulty is encountered. The precise and clear-cut opinion expected of the surgeon turns into a succession of ifs and buts, although clear advice as to necessary action should usually emerge at the end. Perhaps the "diagnostic centres" envisaged by the Minister of Health will so improve facilities that early diagnosis will more frequently be made and, if so, their formation will soon be justified.

GENERAL DIAGNOSTIC INDICATIONS

It is the purpose of this article to examine briefly some of the considerations which may lead to suspicions warranting investigations designed to allay or

medicines will be tried, perhaps with some temporary improvement, and it may not be until the growing carcinoma has begun to ulcerate that gastric analysis, radiography, and finally, perhaps, gastroscopy, will be called in for diagnosis. Even then gastric analysis may mislead, for many patients with gastric cancer are found to have free hydrochloric acid. Hypochlorhydria is the result of gastritis rather than directly of the cancer. Expert radiography can be very helpful, and the more experienced gastroscopists are making rapid advances in accuracy of gastric diagnosis, so that some improvement may begin to be apparent if these examinations are carried out often enough. It is, however, only the alert and careful doctor who will be able to make really effective use of them. He will need to be able to decide when a brief history of loss of appetite and discomfort after food denote serious disease, and when they are merely the transient result of an unhealthy way of life, or are due to psychological causes. Familiarity with the patient's history over many years and with his home surroundings will clearly be of the greatest assistance. A standardized State Medical Service may provide more centres where gastroscopy can be carried out, but it is more likely to decrease than to increase the detailed personal knowledge of patients which is the essential background of diagnostic advance.

THE COLON AND RECTUM

In the large intestine the natural history of cancer pursues a more leisurely course than it does in the stomach, but that is not to say that early diagnosis is any the less necessary. It does, however, imply that diagnosis will be followed by a higher percentage of surgical success.

Cancer of the colon is a disease particularly of middle-aged men and it occurs most frequently in the pelvic colon. But again, the early symptoms are too vague to drive the ordinary well-balanced man to consult his doctor. A slight change in the bowel habit with a greater need for laxatives will not alarm him, and so the earliest stage will be passed over almost unnoticed. Later, when abdominal discomfort increases with periods of distension followed by unexplained attacks of diarrhœa, sometimes accompanied by excess of mucus or even a little blood, the patient is more likely to seek advice, and it is at this point, if not earlier, that the practitioner's suspicions must not fail to be aroused, and examinations by radiography and sigmoido-scope initiated. Digital examination of the rectum must be part of the routine, and respect for the patient's dignity must not prevent the use of the knee-elbow position; so much the best position, especially in stout people, for effective examination to the limit of a finger's reach. In the last resort a decision must be sought by "exploratory laparotomy" so that the whole colon may be passed between the surgeon's fingers. The neoplasms of the colon discovered in these ways will be, on the average, much earlier, in the pathological sense, than the neoplasms of the stomach, so that the results of treatment will be correspondingly better. In the rectum below the level

immediate investigation. In the post-nasal space an early carcinoma may cause no symptoms whatsoever, and frequently it is the presence of secondary glands in the neck that leads to a diagnosis. The same is true of many neoplasms of the tonsil, because they do not ulcerate, and so remain painless until well advanced. The tongue is a common site for cancer, and here there is more hope of early diagnosis because the patient is likely to be aware that there is some abnormality even though the lesion does not hurt. But here, too, the progression from a soft, innocent papilloma or a patch of leucoplakia is insidious and silent, and may easily escape notice except by a trained and careful observer. An extrinsic carcinoma of the larynx, a carcinoma of the pyriform fossa, or a post-cricoid carcinoma are all highly malignant, and in their early stages quite silent. Again, it is often a secondary gland in the neck that first becomes painful and so leads to discovery of a primary lesion that is no longer early. There may be a slight feeling of discomfort in swallowing food, but this is unlikely to induce an otherwise healthy man to consult his doctor. In the œsophagus proper, carcinoma develops most commonly about the level of the bifurcation of the trachea. Routine post-mortem examinations not infrequently show patches of leucoplakia in the œsophagus of middle-aged men, and no doubt a small proportion of these progress to carcinoma. But how many patients will seek medical advice because there is a vague difficulty in swallowing which is painless and difficult to describe or substantiate? By the time there is a real obstruction, with pain referred by the patient very accurately to a point behind the sternum, the disease is advanced, and only a tiny proportion of the lesions are amenable to radical surgery when they are diagnosed. The classical signs are now only too plain: radiography and œsophagoscopy will clinch the matter without much difficulty, but treatment is almost certain to be palliative only.

CARCINOMA OF THE STOMACH

Reference has already been made to the high incidence of cancer of the stomach and its low curability rate. If it were true that a large proportion of gastric cancers were superimposed on chronic ulcers there might be some hope of improving the position, since the ulcers produce symptoms which bring patients to seek medical advice, and even more careful observation of the ulcers might lead to more early discoveries of cancer. Unfortunately, this hope is unfounded.

The great majority of gastric cancers arise unheralded, and the initial symptoms are so vague and inconstant that the diagnosis is seldom made at an early stage. Again, it cannot be claimed that there is a characteristic " clinical picture". In the earliest stage there will literally be no symptoms at all. Afterwards the vague dyspepsia will not for some time convince the patient that he should consult his doctor, nor will this convince the doctor, when he is consulted, that serious investigation is necessary. The standard

medicines will be tried, perhaps with some temporary improvement, and it may not be until the growing carcinoma has begun to ulcerate that gastric analysis, radiography, and finally, perhaps, gastroscopy, will be called in for diagnosis. Even then gastric analysis may mislead, for many patients with gastric cancer are found to have free hydrochloric acid. Hypochlorhydria is the result of gastritis rather than directly of the cancer. Expert radiography can be very helpful, and the more experienced gastroscopists are making rapid advances in accuracy of gastric diagnosis, so that some improvement may begin to be apparent if these examinations are carried out often enough. It is, however, only the alert and careful doctor who will be able to make really effective use of them. He will need to be able to decide when a brief history of loss of appetite and discomfort after food denote serious disease, and when they are merely the transient result of an unhealthy way of life, or are due to psychological causes. Familiarity with the patient's history over many years and with his home surroundings will clearly be of the greatest assistance. A standardized State Medical Service may provide more centres where gastroscopy can be carried out, but it is more likely to decrease than to increase the detailed personal knowledge of patients which is the essential background of diagnostic advance.

THE COLON AND RECTUM

In the large intestine the natural history of cancer pursues a more leisurely course than it does in the stomach, but that is not to say that early diagnosis is any the less necessary. It does, however, imply that diagnosis will be followed by a higher percentage of surgical success.

Cancer of the colon is a disease particularly of middle-aged men and it occurs most frequently in the pelvic colon. But again, the early symptoms are too vague to drive the ordinary well-balanced man to consult his doctor. A slight change in the bowel habit with a greater need for laxatives will not alarm him, and so the earliest stage will be passed over almost unnoticed. Later, when abdominal discomfort increases with periods of distension followed by unexplained attacks of diarrhœa, sometimes accompanied by excess of mucus or even a little blood, the patient is more likely to seek advice, and it is at this point, if not earlier, that the practitioner's suspicions must not fail to be aroused, and examinations by radiography and sigmoidoscope initiated. Digital examination of the rectum must be part of the routine, and respect for the patient's dignity must not prevent the use of the knee-elbow position; so much the best position, especially in stout people, for effective examination to the limit of a finger's reach. In the last resort a decision must be sought by "exploratory laparotomy" so that the whole colon may be passed between the surgeon's fingers. The neoplasms of the colon discovered in these ways will be, on the average, much earlier, in the pathological sense, than the neoplasms of the stomach, so that the results of treatment will be correspondingly better. In the rectum below the level

immediate investigation. In the post-nasal space an early carcinoma may cause no symptoms whatsoever, and frequently it is the presence of secondary glands in the neck that leads to a diagnosis. The same is true of many neoplasms of the tonsil, because they do not ulcerate, and so remain painless until well advanced. The tongue is a common site for cancer, and here there is more hope of early diagnosis because the patient is likely to be aware that there is some abnormality even though the lesion does not hurt. But here, too, the progression from a soft, innocent papilloma or a patch of leucoplakia is insidious and silent, and may easily escape notice except by a trained and careful observer. An extrinsic carcinoma of the larynx, a carcinoma of the pyriform fossa, or a post-cricoid carcinoma are all highly malignant, and in their early stages quite silent. Again, it is often a secondary gland in the neck that first becomes painful and so leads to discovery of a primary lesion that is no longer early. There may be a slight feeling of discomfort in swallowing food, but this is unlikely to induce an otherwise healthy man to consult his doctor. In the œsophagus proper, carcinoma develops most commonly about the level of the bifurcation of the trachea. Routine post-mortem examinations not infrequently show patches of leucoplakia in the œsophagus of middle-aged men, and no doubt a small proportion of these progress to carcinoma. But how many patients will seek medical advice because there is a vague difficulty in swallowing which is painless and difficult to describe or substantiate? By the time there is a real obstruction, with pain referred by the patient very accurately to a point behind the sternum, the disease is advanced, and only a tiny proportion of the lesions are amenable to radical surgery when they are diagnosed. The classical signs are now only too plain: radiography and œsophagoscopy will clinch the matter without much difficulty, but treatment is almost certain to be palliative only.

CARCINOMA OF THE STOMACH

Reference has already been made to the high incidence of cancer of the stomach and its low curability rate. If it were true that a large proportion of gastric cancers were superimposed on chronic ulcers there might be some hope of improving the position, since the ulcers produce symptoms which bring patients to seek medical advice, and even more careful observation of the ulcers might lead to more early discoveries of cancer. Unfortunately, this hope is unfounded.

The great majority of gastric cancers arise unheralded, and the initial symptoms are so vague and inconstant that the diagnosis is seldom made at an early stage. Again, it cannot be claimed that there is a characteristic " clinical picture". In the earliest stage there will literally be no symptoms at all. Afterwards the vague dyspepsia will not for some time convince the patient that he should consult his doctor, nor will this convince the doctor, when he is consulted, that serious investigation is necessary. The standard

medicines will be tried, perhaps with some temporary improvement, and it may not be until the growing carcinoma has begun to ulcerate that gastric analysis, radiography, and finally, perhaps, gastroscopy, will be called in for diagnosis. Even then gastric analysis may mislead, for many patients with gastric cancer are found to have free hydrochloric acid. Hypochlorhydria is the result of gastritis rather than directly of the cancer. Expert radiography can be very helpful, and the more experienced gastroscopists are making rapid advances in accuracy of gastric diagnosis, so that some improvement may begin to be apparent if these examinations are carried out often enough. It is, however, only the alert and careful doctor who will be able to make really effective use of them. He will need to be able to decide when a brief history of loss of appetite and discomfort after food denote serious disease, and when they are merely the transient result of an unhealthy way of life, or are due to psychological causes. Familiarity with the patient's history over many years and with his home surroundings will clearly be of the greatest assistance. A standardized State Medical Service may provide more centres where gastroscopy can be carried out, but it is more likely to decrease than to increase the detailed personal knowledge of patients which is the essential background of diagnostic advance.

THE COLON AND RECTUM

In the large intestine the natural history of cancer pursues a more leisurely course than it does in the stomach, but that is not to say that early diagnosis is any the less necessary. It does, however, imply that diagnosis will be followed by a higher percentage of surgical success.

Cancer of the colon is a disease particularly of middle-aged men and it occurs most frequently in the pelvic colon. But again, the early symptoms are too vague to drive the ordinary well-balanced man to consult his doctor. A slight change in the bowel habit with a greater need for laxatives will not alarm him, and so the earliest stage will be passed over almost unnoticed. Later, when abdominal discomfort increases with periods of distension followed by unexplained attacks of diarrhœa, sometimes accompanied by excess of mucus or even a little blood, the patient is more likely to seek advice, and it is at this point, if not earlier, that the practitioner's suspicions must not fail to be aroused, and examinations by radiography and sigmoidoscope initiated. Digital examination of the rectum must be part of the routine, and respect for the patient's dignity must not prevent the use of the knee-elbow position; so much the best position, especially in stout people, for effective examination to the limit of a finger's reach. In the last resort a decision must be sought by "exploratory laparotomy" so that the whole colon may be passed between the surgeon's fingers. The neoplasms of the colon discovered in these ways will be, on the average, much earlier, in the pathological sense, than the neoplasms of the stomach, so that the results of treatment will be correspondingly better. In the *rectum below the level*

immediate investigation. In the post-nasal space an early carcinoma may cause no symptoms whatsoever, and frequently it is the presence of secondary glands in the neck that leads to a diagnosis. The same is true of many neoplasms of the tonsil, because they do not ulcerate, and so remain painless until well advanced. The tongue is a common site for cancer, and here there is more hope of early diagnosis because the patient is likely to be aware that there is some abnormality even though the lesion does not hurt. But here, too, the progression from a soft, innocent papilloma or a patch of leucoplakia is insidious and silent, and may easily escape notice except by a trained and careful observer. An extrinsic carcinoma of the larynx, a carcinoma of the pyriform fossa, or a post-cricoid carcinoma are all highly malignant, and in their early stages quite silent. Again, it is often a secondary gland in the neck that first becomes painful and so leads to discovery of a primary lesion that is no longer early. There may be a slight feeling of discomfort in swallowing food, but this is unlikely to induce an otherwise healthy man to consult his doctor. In the œsophagus proper, carcinoma develops most commonly about the level of the bifurcation of the trachea. Routine post-mortem examinations not infrequently show patches of leucoplakia in the œsophagus of middle-aged men, and no doubt a small proportion of these progress to carcinoma. But how many patients will seek medical advice because there is a vague difficulty in swallowing which is painless and difficult to describe or substantiate? By the time there is a real obstruction, with pain referred by the patient very accurately to a point behind the sternum, the disease is advanced, and only a tiny proportion of the lesions are amenable to radical surgery when they are diagnosed. The classical signs are now only too plain: radiography and œsophagoscopy will clinch the matter without much difficulty, but treatment is almost certain to be palliative only.

CARCINOMA OF THE STOMACH

Reference has already been made to the high incidence of cancer of the stomach and its low curability rate. If it were true that a large proportion of gastric cancers were superimposed on chronic ulcers there might be some hope of improving the position, since the ulcers produce symptoms which bring patients to seek medical advice, and even more careful observation of the ulcers might lead to more early discoveries of cancer. Unfortunately, this hope is unfounded.

The great majority of gastric cancers arise unheralded, and the initial symptoms are so vague and inconstant that the diagnosis is seldom made at an early stage. Again, it cannot be claimed that there is a characteristic " clinical picture". In the earliest stage there will literally be no symptoms at all. Afterwards the vague dyspepsia will not for some time convince the patient that he should consult his doctor, nor will this convince the doctor, when he is consulted, that serious investigation is necessary. The standard

medicines will be tried, perhaps with some temporary improvement, and it may not be until the growing carcinoma has begun to ulcerate that gastric analysis, radiography, and finally, perhaps, gastroscopy, will be called in for diagnosis. Even then gastric analysis may mislead, for many patients with gastric cancer are found to have free hydrochloric acid. Hypochlorhydria is the result of gastritis rather than directly of the cancer. Expert radiography can be very helpful, and the more experienced gastroscopists are making rapid advances in accuracy of gastric diagnosis, so that some improvement may begin to be apparent if these examinations are carried out often enough. It is, however, only the alert and careful doctor who will be able to make really effective use of them. He will need to be able to decide when a brief history of loss of appetite and discomfort after food denote serious disease, and when they are merely the transient result of an unhealthy way of life, or are due to psychological causes. Familiarity with the patient's history over many years and with his home surroundings will clearly be of the greatest assistance. A standardized State Medical Service may provide more centres where gastroscopy can be carried out, but it is more likely to decrease than to increase the detailed personal knowledge of patients which is the essential background of diagnostic advance.

THE COLON AND RECTUM

In the large intestine the natural history of cancer pursues a more leisurely course than it does in the stomach, but that is not to say that early diagnosis is any the less necessary. It does, however, imply that diagnosis will be followed by a higher percentage of surgical success.

Cancer of the colon is a disease particularly of middle-aged men and it occurs most frequently in the pelvic colon. But again, the early symptoms are too vague to drive the ordinary well-balanced man to consult his doctor. A slight change in the bowel habit with a greater need for laxatives will not alarm him, and so the earliest stage will be passed over almost unnoticed. Later, when abdominal discomfort increases with periods of distension followed by unexplained attacks of diarrhœa, sometimes accompanied by excess of mucus or even a little blood, the patient is more likely to seek advice, and it is at this point, if not earlier, that the practitioner's suspicions must not fail to be aroused, and examinations by radiography and sigmoidoscope initiated. Digital examination of the rectum must be part of the routine, and respect for the patient's dignity must not prevent the use of the knee-elbow position; so much the best position, especially in stout people, for effective examination to the limit of a finger's reach. In the last resort a decision must be sought by "exploratory laparotomy" so that the whole colon may be passed between the surgeon's fingers. The neoplasms of the colon discovered in these ways will be, on the average, much earlier, in the pathological sense, than the neoplasms of the stomach, so that the results of treatment will be correspondingly better. In the rectum below the level

immediate investigation. In the post-nasal space an early carcinoma may cause no symptoms whatsoever, and frequently it is the presence of secondary glands in the neck that leads to a diagnosis. The same is true of many neoplasms of the tonsil, because they do not ulcerate, and so remain painless until well advanced. The tongue is a common site for cancer, and here there is more hope of early diagnosis because the patient is likely to be aware that there is some abnormality even though the lesion does not hurt. But here, too, the progression from a soft, innocent papilloma or a patch of leucoplakia is insidious and silent, and may easily escape notice except by a trained and careful observer. An extrinsic carcinoma of the larynx, a carcinoma of the pyriform fossa, or a post-cricoid carcinoma are all highly malignant, and in their early stages quite silent. Again, it is often a secondary gland in the neck that first becomes painful and so leads to discovery of a primary lesion that is no longer early. There may be a slight feeling of discomfort in swallowing food, but this is unlikely to induce an otherwise healthy man to consult his doctor. In the œsophagus proper, carcinoma develops most commonly about the level of the bifurcation of the trachea. Routine post-mortem examinations not infrequently show patches of leucoplakia in the œsophagus of middle-aged men, and no doubt a small proportion of these progress to carcinoma. But how many patients will seek medical advice because there is a vague difficulty in swallowing which is painless and difficult to describe or substantiate? By the time there is a real obstruction, with pain referred by the patient very accurately to a point behind the sternum, the disease is advanced, and only a tiny proportion of the lesions are amenable to radical surgery when they are diagnosed. The classical signs are now only too plain: radiography and œsophagoscopy will clinch the matter without much difficulty, but treatment is almost certain to be palliative only.

CARCINOMA OF THE STOMACH

Reference has already been made to the high incidence of cancer of the stomach and its low curability rate. If it were true that a large proportion of gastric cancers were superimposed on chronic ulcers there might be some hope of improving the position, since the ulcers produce symptoms which bring patients to seek medical advice, and even more careful observation of the ulcers might lead to more early discoveries of cancer. Unfortunately, this hope is unfounded.

The great majority of gastric cancers arise unheralded, and the initial symptoms are so vague and inconstant that the diagnosis is seldom made at an early stage. Again, it cannot be claimed that there is a characteristic " clinical picture". In the earliest stage there will literally be no symptoms at all. Afterwards the vague dyspepsia will not for some time convince the patient that he should consult his doctor, nor will this convince the doctor, when he is consulted, that serious investigation is necessary. The standard

REVISION CORNER

This section is devoted to short articles in which experts summarize modern treatment and clinical procedures, particularly for the benefit of general practitioners who have returned from the Forces.

THE TREATMENT OF TOXIC GOITRE (Thyrotoxicosis)

IN toxic goitre there is excessive secretion by the thyroid gland. This is the cause of the symptoms whatever the age of the patient, whether the gland is smooth or nodular, and whether the toxic symptoms appear at the same time as the goitre or later. Therefore, from the point of view of treatment, all cases can be included in a single category, namely toxic goitre, and there is little to be gained by classification. The most rational treatment, removal of the cause, is impossible at present, as it is unknown, although there is now good evidence that stimulation by the pituitary is the immediate cause of hyperthyroidism. However, measures to control the thyroid through the pituitary have not been successful, and the methods used to reduce the secretion of the thyroid are still aimed at the gland itself. The chief ones are drugs, surgical removal, and irradiation, either alone or in combination. In drug and irradiation therapy there have lately been important developments. In 1943, new antithyroid drugs, substances which interfere with the synthesis of thyroxine within the gland, were discovered and used clinically; and within the last few years radio-active iodine also, when given by mouth, has been found to have powerful effects in reducing thyroid activity. Before the recent advances in drug therapy, iodine was mainly relied upon, but this was rarely able to produce a satisfactory and permanent effect upon the disease. The new anti-thyroid drugs, of which thiouracil and methyl thiouracil are the most useful so far, are both more potent and more permanent in their effects. With rare exceptions they are able to reduce the over-production of thyroxine to a normal level, and if the dose is not adjusted, to a subnormal level, so that myxœdema will occur. Detailed discussion of the diagnosis is not included here, but it must be mentioned that thiouracil has no favourable effect upon those symptoms of neurosis which simulate toxic goitre, neither should it be given to patients showing eye signs, such as proptosis and lid retraction, but none of the other symptoms associated with toxic goitre.

THIOURACIL

Thiouracil has two chief drawbacks—the necessity of giving it over long periods, and the frequent occurrence of toxic reactions. Efforts are being made to overcome the last defect by seeking a less toxic drug, or some substance which when given with thiouracil will have a protective action on the tissues.

Dosage.—Thiouracil (or methyl thiouracil) is used as follows: 0.2 gm. t.i.d. for an initial period of about three weeks; then 0.1 gm. t.i.d. for a few weeks, and then possibly a further reduction to the maintenance dose, which varies from 0.1 gm. daily to 0.1 gm t.i.d. This maintenance dose may be no longer required after a few months, but after an interval without treatment, varying from a few weeks to a few months, it is likely that symptoms will recur, and the drug will again have to be given. Supervision should be fairly close during the initial weeks of treatment, first at intervals of a few days, then lengthening to a week or two. The best guides to the action of the drug are weight, pulse rate, feeling of well-being, steadiness, and ability to work. It is noteworthy that in the older patients appetites improve as thyroid toxæmia lessens. In a patient previously untreated great improvement can be expected in the first month, and in most cases the basal metabolism will have reached normal limits within six weeks. The period required to restore a patient to normal health will increase in proportion to the severity of the initial condition, but even in a severe case this can be accomplished in three months.

of the peritoneal reflection diagnosis does, on the whole, tend to be made earlier than when the disease is higher up, since the symptoms—frequent watery evacuations with mucus or blood—will soon become noticeable. Even so it is a constant source of astonishment to any proctologist how many of these easily detected neoplasms do, as a matter of fact, reach an advanced stage before they are diagnosed. All are within reach of a finger, all produce symptoms quite early. The explanation of failure on the medical side, if there is any, is perhaps a reluctance to carry out a digital examination often enough, because of the feeling that so many examinations will be negative—although one early diagnosis is worth a hundred finger-stalls in the waste paper basket!

Cancer of the rectum.—At the lower end of the rectum, that is in the anal canal or anal margin, a malignant neoplasm is uncommon, but is at least capable of being diagnosed early. It will cause irritation and a blood-stained, purulent discharge almost from the first, and should not escape the notice of any careful observer. It is almost, if not quite, an "external cancer", in which as a class diagnosis should be much earlier than is ever likely to be possible in "internal cancer".

CONCLUSION

This brief survey of the difficulties in the way of early diagnosis of malignant disease, is depressing in its continual insistence on the unlikeliness of most patients seeking advice in the really early stages of the disease. It serves to emphasize, however, how necessary it is for every practitioner to be in a perpetual state of watchfulness : full of suspicions which even long experience should not tend to replace by complacency; alert to act on suspicion even when many examinations will prove negative. The practitioner's mind should almost, in fact, be in a state of "cancer-phobia" on his patient's behalf. An attitude which is pathological if it fills a man's mind with regard to himself, may be wholly beneficial if it is directed towards the welfare of other people. The practitioner who is always a complacent optimist will do grave injury to his patient if he dismisses his suspicions because they are only suspicions. Certainty one way or the other must always be his aim, and this certainty must be achieved without delay.

the disease well, and included in its effects are the restoration of normal rhythm and the disappearance of congestive failure. Such patients are quite content to take the drug for long periods rather than undergo operation, the risks of which are greater in the elderly, even though they will be less after preparation with thiouracil.

The diagnostic value of thiouracil.—A subsidiary use for thiouracil, which has become apparent since it was established as a reliable drug for counteracting hyperthyroidism, is its value as a diagnostic agent. It is sometimes impossible to say whether or not thyroid overaction is present, and if so to what extent it is causing the symptoms. In such cases a trial of thiouracil can often settle the problem.

RADIO-ACTIVE IODINE

Radio-active idoine has recently been used in the United States to treat toxic goitre, with considerable success, although only small numbers have so far been reported. The radio-activity is produced in a cyclotron, and the iodine thus prepared must be taken by mouth within a few hours, as the radio-activity is rapidly lost. A small quantity of almost tasteless liquid is drunk containing less than 2 mgm. of radio-active iodine, the majority of which is quickly taken up by the thyroid. Reduction of the B.M.R. to normal is reported in one to five months, and in many cases the thyroid shrinks to normal size. As drawbacks to the method there is first the minor one of slight toxic effects lasting only a day or two after the administration, and the occurrence later of myxœdema, due to an excessive dose of the radio-active element. This internal radiotherapy is still in an experimental stage, but shows promise, and has the advantage of being the simplest, from the patient's point of view, yet used.

CONCLUSION

To sum up the present position in the treatment of toxic goitre, no method is ideal and each has its drawbacks as well as advantages. Surgical removal of the goitre after preparation with thiouracil and iodine will give satisfactory results, and is especially suitable for young patients and for those with large goitres. Thyroidectomy is imperative if the gland is causing pressure symptoms. It will also probably be required if treatment with thiouracil has to be given up because of toxic symptoms. Thiouracil has a place as the sole method of treatment, more especially in the elderly or in those with cardiovascular disease, or any other condition which renders operation unduly hazardous. It may be tried in the young with mild symptoms, and in any patient who has a recurrence of the disease after thyroidectomy.

HAROLD COOKSON, M.D., F.R.C.P.

THE Rh FACTOR

THE important discovery of the standard blood groups by Carl Landsteiner in 1900, which made possible the safe transfusion of blood, was the forerunner of the demonstration of increasing numbers of subdivisions in human blood. By 1928 the number of known subdivisions had increased from four to thirty-six, although only the original four were of practical importance. In 1940, Landsteiner and Wiener found that injections of red blood cells of the rhesus monkey into a rabbit produced an anti-serum which not only reacted with the original rhesus monkey cells but also agglutinated the red cells of human beings. These human red cells therefore contained the agglutinogen which was present in the red cells of the rhesus monkey. This was designated the rhesus or Rh factor. The cells of 85 per cent. of the white populations of Britain and the U.S.A. were found to contain the agglutinogen and such people were called Rh-positive; 15 per cent. were Rh-negative.

THE PROCESS OF ANTISERA FORMATION

Transmission of the agglutinogen into the circulation of Rh-negative humans produced an agglutinin: anti-Rh serum. This serum in contact with Rh-positive cells agglutinated and hæmolysed them. Although the Rh factor is transmitted as a

The chief *toxic effects* are pain in the neck and joints, pyrexia, rashes, malaise, gastro-interstinal disturbances, headaches, œdema of the feet, and depression of the leucocytes. It is rare for these toxic effects to occur within the first few days, but they sometimes develop at the end of the first week, or may develop at any future date, even after a year or two. With pyrexia and neck pains, the most common reactions, the drug is best abandoned. A rash may clear up if the drug is stopped for a few days or given in reduced amount. The only serious reaction is agranulocytosis, which has led to a few fatalities. This is most likely to develop within the first month or two, but can occur at any later period. The first warning of it is usually a sore throat and if this or any other adverse symptom should appear, a white count must be done. Many authors advise that white counts should be done frequently, as often as every second day, during the initial weeks of treatment, but it is doubtful if this is worth while, and it puts a heavy strain on the laboratory if many cases are being treated. I do not resort to frequent routine white counts, but impress on the patient the necessity of stopping the drug immediately if any untoward symptoms should develop, and in particular a sore throat. The patient must then report for investigation, which will include a blood count. More frequent than agranulocytosis is granulopenia, with a moderate reduction of the polymorphonuclear cells and without any evidence of infection. When this is found the drug should be omitted for a few days, when the white count is likely to increase to normal. Thiouracil may then be resumed in small doses, the effect on the leucocytes being watched. An increase in size and in the hardness of the thyroid often occurs, and is classed as a toxic effect by some, although it is more correctly regarded as evidence of the action of thiouracil where it is wanted, that is on the thyroid itself. Such effects can be lessened by reducing the dose of the drug or giving a little thyroid extract, ½ grain (32 mgm.) once or twice a day. It is time to advise removal of any goitre which is causing pressure symptoms, whether toxic or not.

Thouracil in conjunction with surgery.—The question arises as to how the advent of thiouracil alters the management of toxic goitre. To consider first the situation before its introduction, there were a few mild cases which could be maintained in fair health by iodine and limited activity, but this method could not be relied upon to restore good health. The best treatment was a subtotal thyroidectomy after a period of preparation with iodine, rest, and standard measures for heart failure, if this existed. Excellent results were obtained, but sometimes the patient could not be brought to a state in which operation could be done with reasonable safety. In such patients operation was withheld, and death eventually occurred, or thyroidectomy was carried out, with considerable mortality. Now it should be possible, with rare exceptions, to detoxicate a patient completely with thiouracil and iodine before an operation, so that the risk is less then ever before. This is the part which thiouracil can play in combination with surgery. The technique is as follows :—

Thiouracil is given in the dosage already described, that is, 0.2 gm. three times daily for three or four weeks, and then reduced to 0.1 gm. t.i.d.; when the metabolic rate is about +20 per cent. Lugol's iodine, 10 minims (0.6 c.cm.) t.i.d., is given in addition. Then, after a further period, when the B.M.R. is about normal, thyroidectomy is carried out, and as thiouracil lowers metabolism on the average at the rate of 1 per cent. daily (although there are wide variations) this means that the patient will be fit for operation about two weeks after starting iodine. The reason for the pre-operative use of iodine as a supplement to thiouracil is that the latter causes increased vascularity of the gland and troublesome bleeding. Iodine counteracts this effect to some extent.

There is also a place for *thiouracil as the sole form of treatment*. In the young, with a goitre which is toxic, but not too large, prolonged treatment with the drug may cure the symptoms and eventually cause disappearance of the goitre. In elderly women, in whom toxic goitre is all too common, and is often accompanied by auricular fibrillation and congestive heart failure, thiouracil is found to control

the disease well, and included in its effects are the restoration of normal rhythm and the disappearance of congestive failure. Such patients are quite content to take the drug for long periods rather than undergo operation, the risks of which are greater in the elderly, even though they will be less after preparation with thiouracil.

The diagnostic value of thiouracil.—A subsidiary use for thiouracil, which has become apparent since it was established as a reliable drug for counteracting hyperthyroidism, is its value as a diagnostic agent. It is sometimes impossible to say whether or not thyroid overaction is present, and if so to what extent it is causing the symptoms. In such cases a trial of thiouracil can often settle the problem.

RADIO-ACTIVE IODINE

Radio-active idoine has recently been used in the United States to treat toxic goitre, with considerable success, although only small numbers have so far been reported. The radio-activity is produced in a cyclotron, and the iodine thus prepared must be taken by mouth within a few hours, as the radio-activity is rapidly lost. A small quantity of almost tasteless liquid is drunk containing less than 2 mgm. of radio-active iodine, the majority of which is quickly taken up by the thyroid. Reduction of the B.M.R. to normal is reported in one to five months, and in many cases the thyroid shrinks to normal size. As drawbacks to the method there is first the minor one of slight toxic effects lasting only a day or two after the administration, and the occurrence later of myxœdema, due to an excessive dose of the radio-active element. This internal radiotherapy is still in an experimental stage, but shows promise, and has the advantage of being the simplest, from the patient's point of view, yet used.

CONCLUSION

To sum up the present position in the treatment of toxic goitre, no method is ideal and each has its drawbacks as well as advantages. Surgical removal of the goitre after preparation with thiouracil and iodine will give satisfactory results, and is especially suitable for young patients and for those with large goitres. Thyroidectomy is imperative if the gland is causing pressure symptoms. It will also probably be required if treatment with thiouracil has to be given up because of toxic symptoms. Thiouracil has a place as the sole method of treatment, more especially in the elderly or in those with cardiovascular disease, or any other condition which renders operation unduly hazardous. It may be tried in the young with mild symptoms, and in any patient who has a recurrence of the disease after thyroidectomy.

HAROLD COOKSON, M.D., F.R.C.P.

THE Rh FACTOR

THE important discovery of the standard blood groups by Carl Landsteiner in 1900, which made possible the safe transfusion of blood, was the forerunner of the demonstration of increasing numbers of subdivisions in human blood. By 1928 the number of known subdivisions had increased from four to thirty-six, although only the original four were of practical importance. In 1940, Landsteiner and Wiener found that injections of red blood cells of the rhesus monkey into a rabbit produced an anti-serum which not only reacted with the original rhesus monkey cells but also agglutinated the red cells of human beings. These human red cells therefore contained the agglutinogen which was present in the red cells of the rhesus monkey. This was designated the rhesus or Rh factor. The cells of 85 per cent. of the white populations of Britain and the U.S.A. were found to contain the agglutinogen and such people were called Rh-positive; 15 per cent. were Rh-negative.

THE PROCESS OF ANTISERA FORMATION

Transmission of the agglutinogen into the circulation of Rh-negative humans produced an agglutinin: anti-Rh serum. This serum in contact with Rh-positive cells agglutinated and hæmolysed them. Although the Rh factor is transmitted as a

Mendelian dominant, the antisera are not hereditarily transmitted, as are the antisera to the normal blood groups, but are only produced in response to the introduction of the agglutinogen by blood transfusion or during pregnancy. The blood of an Rh-negative mother with an Rh-positive husband and Rh-positive fœtus, produces an anti-Rh serum which is transmitted to the fœtal circulation and may there agglutinate the fœtal red blood cells. Work on these human antisera demonstrated that some of them agglutinated cells which were not agglutinated by the original rabbit's serum. Three separate antisera were at first isolated. Therefore the conception that there was a single specific Rh agglutinogen failed and two additional variations were found. These agglutinogens may occur singly or in combination (just as the A and B factors in the standard blood groups in combination produce a group AB) and give rise to eight possible types of blood as demonstrated in table 1.

TABLE I

To show the method of identification of Rh groups using three standard sera (Wiener, A. S. (1945): *J. Lab. clin. Med.*, **30**, 957).

Rh Group	Reaction with standard sera		
	Anti-Rh′	Anti-Rh″	Anti-Rh$_0$
Rh-negative	—	—	—
Rh$_0$	—	—	+
Rh′	+	—	—
Rh″	—	+	—
Rh′ Rh″	+	+	—
Rh′$_0$	+	—	+
Rh″$_0$	—	+	+
Rh′$_0$ Rh″$_0$	+	+	+

Later, brilliant research by Race and Taylor revealed the existence of a fourth specific antiserum, thereby increasing the number of detectable Rh groups to 12. Study of the hereditary transmission of agglutinogens in families has established the existence of two further agglutinogens against which specific antisera have not yet been isolated. This again increases the theoretical number of Rh groups and it is probable that these total 36, although the majority cannot yet be detected. Classification of these Rh groups in England depends upon the standard sera which agglutinate unknown cells. For example, in my laboratory cells which are agglutinated by standard sera numbered 1, 3 and 4 would be designated Rh 134.

THE CLINICAL APPLICATIONS OF KNOWLEDGE OF THE RH FACTOR

The clinical importance of the Rh factor is concerned with the formation of anti-Rh agglutinins. As stated above, they are not naturally transmitted but are only produced artificially during pregnancy and following blood transfusion.

During pregnancy, antibodies may be formed in the maternal circulation in response to the presence of an Rh-positive fœtus. The maternal antibodies so formed, pass back into the circulation of the fœtus and there may react with the fœtal Rh-positive cells, producing a hæmolytic reaction. Individuals differ considerably in the ease with which they can produce antibodies, and on an average only 1:25 Rh-negative individuals, exposed to Rh antigen, produces antiserum. Every additional exposure after the first increases the risk of antibody formation. The mating of Rh-positive men with Rh-negative women occurs approximately in 1 out

of every 10 marriages (Wiener, 1945). Therefore only 1 out of every 250 marriages results in antibody production to a significant degree. In those which do, the first-born is likely to be unaffected, unless the woman has had a previous blood transfusion with Rh-positive blood, but each successive pregnancy increases the risk of fœtal hæmolytic disease.

The diseases to which the Rh antigen-agglutinin reaction may give rise are grouped under the general term "erythroblastosis fœtalis" and are in particular:—

(1) Macerated fœtus
(2) Hydrops fœtalis
(3) Icterus gravis neonatorum
(4) Congenital anæmia

It is advisable that all pregnant women and their husbands be grouped in respect of Rh factors and particularly is it important when a history is elicited of previous blood transfusion to the mother or one of the above conditions during a previous pregnancy. When the husband is Rh-positive and the wife Rh-negative, it is advisable that the pregnancy be terminated as soon as a viable child can be expected. This measure withdraws the child from the maternal antibodies. *There is at present no known way of desensitizing the mother.* In addition, antibodies can be transmitted to the fœtal circulation in maternal milk, so that breast feeding should not be instituted unless other overriding considerations are present.

The treatment of a child with one of the forms of erythroblastosis fœtalis is blood transfusion with group O blood of the same Rh subgroup.

In blood transfusion, Rh agglutinogen may be transmitted to a recipient who may then produce Rh antibodies. As a result, transfused cells containing the agglutinogen may be destroyed and the hæmoglobin of the recipient may not rise by the anticipated amount, or indeed may not rise at all. Ideally, all Rh-negative recipients should be transfused only with Rh-negative blood. Such a course is not practicable at the moment but should be followed when the recipient is a woman of child-bearing age, or an infant with erythroblastosis fœtalis. Finally, those patients who require multiple or repeated transfusion for red cell replacement, should be grouped in respect of the Rh factor.

<div align="right">A. KEKWICK, M.B., F.R.C.P.</div>

INDICATIONS FOR ELECTRO-CONVULSIVE THERAPY

CONVULSION therapy has an almost specific remedial effect in one circumscribed psychiatric syndrome, but as generally used in psychiatry it is a symptomatic method for the treatment of depression. Almost any departure of the organism from a state of normal health is likely to be reflected in a feeling of depression. It may occur as a symptom in bodily illnesses of all kinds, and in all major psychiatric disorders, including schizophrenia and general paralysis, as well as being a reaction of the normal individual to the griefs and disappointments of everyday life. In only a few of these conditions is convulsion therapy likely to be needed. Individuals vary considerably in the way they feel depressed. Most people would describe their feelings as those of unhappiness or misery; but others would find it truer to say that they felt apathetic, uninterested or even tired. In a depressed state some people become restless, anxious or agitated, others quiet and still, with a demonstrable slowing of thought and action. Thus it is often not easy to decide clinically when a patient is suffering from a state which can and should be treated by convulsion therapy.

The involutional depressive state.—The syndrome in which convulsion therapy produces its most striking benefits is the involutional depressive state. Claims of up to 90 per cent. of cures have been made with this disease. It is both common and severe, and as it may last for years before spontaneous recovery, convulsion therapy is called for unless there are the strongest contraindications. Characteristically, the illness comes on insidiously, and usually for no apparent reason, in the fifth and sixth decades, most frequently in men and women of the "obsessional" type of

Mendelian dominant, the antisera are not hereditarily transmitted, as are the antisera to the normal blood groups, but are only produced in response to the introduction of the agglutinogen by blood transfusion or during pregnancy. The blood of an Rh-negative mother with an Rh-positive husband and Rh-positive fœtus, produces an anti-Rh serum which is transmitted to the fœtal circulation and may there agglutinate the fœtal red blood cells. Work on these human antisera demonstrated that some of them agglutinated cells which were not agglutinated by the original rabbit's serum. Three separate antisera were at first isolated. Therefore the conception that there was a single specific Rh agglutinogen failed and two additional variations were found. These agglutinogens may occur singly or in combination (just as the A and B factors in the standard blood groups in combination produce a group AB) and give rise to eight possible types of blood as demonstrated in table 1.

TABLE I

To show the method of identification of Rh groups using three standard sera (Wiener, A. S. (1945): *J. Lab. clin. Med.*, **30**, 957).

	Reaction with standard sera		
Rh Group	Anti-Rh'	Anti-Rh"	Anti-Rh_0
Rh-negative	—	—	—
Rh_0	—	—	+
Rh'	+	—	—
Rh"	—	+	—
Rh' Rh"	+	+	—
Rh'_0	+	—	+
$Rh"_0$	—	+	+
Rh'_0 $Rh"_0$	+	+	+

Later, brilliant research by Race and Taylor revealed the existence of a fourth specific antiserum, thereby increasing the number of detectable Rh groups to 12. Study of the hereditary transmission of agglutinogens in families has established the existence of two further agglutinogens against which specific antisera have not yet been isolated. This again increases the theoretical number of Rh groups and it is probable that these total 36, although the majority cannot yet be detected. Classification of these Rh groups in England depends upon the standard sera which agglutinate unknown cells. For example, in my laboratory cells which are agglutinated by standard sera numbered 1, 3 and 4 would be designated Rh 134.

THE CLINICAL APPLICATIONS OF KNOWLEDGE OF THE RH FACTOR

The clinical importance of the Rh factor is concerned with the formation of anti-Rh agglutinins. As stated above, they are not naturally transmitted but are only produced artificially during pregnancy and following blood transfusion.

During pregnancy, antibodies may be formed in the maternal circulation in response to the presence of an Rh-positive fœtus. The maternal antibodies so formed, pass back into the circulation of the fœtus and there may react with the fœtal Rh-positive cells, producing a hæmolytic reaction. Individuals differ considerably in the ease with which they can produce antibodies, and on an average only 1:25 Rh-negative individuals, exposed to Rh antigen, produces antiserum. Every additional exposure after the first increases the risk of antibody formation. The mating of Rh-positive men with Rh-negative women occurs approximately in 1 out

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Transport of Pregnant Woman by Air

QUERY.—A seven months' pregnant woman is obliged to go on a long journey travelling by air. How great a risk is there of precipitating a premature labour? Would progesterone given beforehand be of any value in preventing this? What precautions should be recommended in such a case?

REPLY.—The risk of precipitating premature labour as a result of a long journey by air is extremely slight; in many cases much less than by other forms of transport. Certain factors should, however, be borne in mind of which the more important are:—

(a) *The length of flight.*—A long flight in bad or indifferent weather can be very fatiguing and exhausting.

(b) *The greatest height at which the aircraft may be flown; and whether or not oxygen is available.*—It is presumed that oxygen requirements of a pregnant woman are greater than those of other persons, and she is consequently more subject to anoxia. Adequate supplies should therefore be readily available if it is anticipated that the aircraft will fly at a greater height than 10,000 feet.

There is little previous experience on which a clear-cut policy can be enunciated, and present decisions may have to be modified in the light of experience. It is of interest to note that at a recent conference of the Airline Medical Directors Association of America, at which I was present, it was unanimously decided to accept women for transportation by air up to and including the eighth month of pregnancy. This decision was based on the experience gained to date by the airline companies operating in America.

It is not considered that progesterone would be of any use in preventing premature labour in such cases. Were labour to be precipitated during flight, the cause would be a mechanical one brought about by meteorological disturbances, over which endocrine therapy would have no control. No special precautions, other than those normally taken by a pregnant woman when travelling, need be observed, apart from those recommended for all travellers by air.

KENNETH G. BERGIN, M.D.
Assistant Director Medical Services,
British Overseas Airways Corporation.

Prophylaxis of the Common Cold

QUERY.—I should be grateful if you could tell me which is the best preventive for winter colds. Are the sulphonamides or penicillin of any value?

REPLY.—No effective prophylactic against winter colds is known. *Bacterial vaccines* of various sorts have had a wide vogue, but no statistical evidence of their value has ever been obtained in a satisfactorily controlled investigation. Ultra-violet light and vitamins, especially A and D, have also been employed, but with these again, although some workers have claimed good results especially with ultra-violet light, no statistically satisfactory evidence of their value has been obtained.

With regard to the *sulphonamides*, the experience of the United States armed forces, especially the Navy, is of interest. Preliminary reports of the use of sulphonamides, in dosages of 0.5 to 1.0 gm. daily, in the prophylaxis of epidemic respiratory infections showed a statistically significant diminution in hæmolytic streptococcal infections, but further experience showed that the organisms became sulphonamide-fast, and in many centres even worse epidemics then occurred than had been observed before the use of sulphonamide prophylaxis. The diminution in respiratory infections in the earlier part of this investigation applied only to streptococcal infections and not to the common cold, which is generally accepted as a virus infection.

No information is available about the prophylactic value of *penicillin* against respiratory infections in general. *A priori* it might be expected that penicillin would be effective only against infections by streptococci and other penicillin-sensitive bacteria; there has been no evidence that penicillin has any effect against virus infections. The only practicable way of using penicillin prophylactically would be in the form of lozenges. It is conceivable that these might be of value in the presence of an epidemic of streptococcal infections, but it is improbable that they would diminish the liability to virus infections.

In any patient who seems to be unduly liable to the common cold the question of an allergic background or of chronic infections of the nasal sinuses should be investigated.

J. G. SCADDING, M.D., F.R.C.P.

The Treatment of Black Hairy Tongue

QUERY.—In November 1945, a lady farmer noticed that her tongue was covered with a black fur especially marked over the posterior third. In July 1946, a swab was taken and the

personality. They are careful, orderly, conscientious people, and some of the world's best citizens, although they tend to suffer from a certain inflexibility of character. In its earliest stages, the illness may present the picture of a "neurasthenia", and be thought to be due to a spell of overwork or the minor domestic worries from which few are free. As the depression deepens, however, it soon shows itself to be too excessive to be regarded as a normal psychological reaction. Treatment should be begun as soon as a safe diagnosis can be made, as response is quicker and more favourable in the early stages. Persons of the obsessional type are rather more liable to lasting spells of depression than most of mankind. They may suffer in this way earlier in life than the involutional period, and if the gravity of the symptoms warrants it, the response to convulsion treatment will probably be good.

Manic-depressive psychosis.—Depression is the cardinal symptom of the depressive phase of a manic-depressive psychosis. The type of personality most susceptible to this is very different from the obsessional one, and is rather of the active, sociable, expansive kind, usually full of good spirits but at times liable to fits of the blues, which seem to come from nowhere and may last only a short time. At intervals, however, a mood change, which starts in the usual way for them, does not clear up but progresses rapidly to an extreme degree of melancholy. In a lifetime there may be many attacks, and a rhythmic quality can often be found. Other relatives may also have suffered in a similar way. Eventually, the attacks almost invariably remit on their own, unless such an accident as suicide intervenes. But while life continues there is always the possibility of relapse. Convulsion treatment must be considered in these illnesses, although it is not so promising as in the involutional depression. Often only temporary benefit is obtained, and the patient relapses every time the treatment is discontinued until the natural term of the existing phase has been reached. As the total amount of convulsion therapy which it is justifiable to give to one patient is limited, it is often wise in manic-depressive illnesses to postpone treatment for a while until it can be hoped that the therapeutically induced remission will be carried on into spontaneous recovery.

Depression is a normal reaction to depressing events; and if the personality is one lacking in resilience the reaction may take on a disabling permanence and severity. It is important that the patient's life should be explored for the causes of the depression. If causes can be found, they should be dealt with on their own merits, by social readjustments of various kinds, or by some simple psychotherapy. However, if all possible steps of this kind have been taken, and the patient still remains ill, convulsion therapy may be the crucial factor in breaking the vicious circle.

Convulsion therapy is of occasional use in many other conditions, such as certain schizophrenic states, but the indications depend so much upon individual factors that general rules cannot easily be laid down.

SOME CONTRAINDICATIONS

Although the depression, to which the obsessional personality is liable, responds well to convulsion treatment, the underlying personality remains unaffected; and it is useless to try to treat obsessional neuroses in this way. The same is true of anxiety neuroses; and anxiety is made worse by the treatment in whatever kind of illness it is found. Considerable caution should be exercised with the elderly or the arteriosclerotic patient. When there is any organic impairment of the brain, memory is likely to deteriorate under the treatment, and confusional episodes may ensue. Convulsion treatment long continued affects the memory of nearly all patients, and "courses" of treatment should not as a rule be planned. Instead, the patient should receive only the minimum number of fits required to start him well on the road to recovery. His response to the first two treatments will usually indicate what can be expected. Finally, it must be remembered that convulsion therapy puts a strain on the heart and the bones, especially the vertebræ, as well as on the brain. When these are diseased special precautions are needed, if the treatment is to be given at all.

ELIOT SLATER, M.D., F.R.C.P.

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Transport of Pregnant Woman by Air

QUERY.—A seven months' pregnant woman is obliged to go on a long journey travelling by air. How great a risk is there of precipitating a premature labour? Would progesterone given beforehand be of any value in preventing this? What precautions should be recommended in such a case?

REPLY.—The risk of precipitating premature labour as a result of a long journey by air is extremely slight; in many cases much less than by other forms of transport. Certain factors should, however, be borne in mind of which the more important are:—

(a) *The length of flight.*—A long flight in bad or indifferent weather can be very fatiguing and exhausting.

(b) *The greatest height at which the aircraft may be flown; and whether or not oxygen is available.*— It is presumed that oxygen requirements of a pregnant woman are greater than those of other persons, and she is consequently more subject to anoxia. Adequate supplies should therefore be readily available if it is anticipated that the aircraft will fly at a greater height than 10,000 feet.

There is little previous experience on which a clear-cut policy can be enunciated, and present decisions may have to be modified in the light of experience. It is of interest to note that at a recent conference of the Airline Medical Directors Association of America, at which I was present, it was unanimously decided to accept women for transportation by air up to and including the eighth month of pregnancy. This decision was based on the experience gained to date by the airline companies operating in America.

It is not considered that progesterone would be of any use in preventing premature labour in such cases. Were labour to be precipitated during flight, the cause would be a mechanical one brought about by meteorological disturbances, over which endocrine therapy would have no control. No special precautions, other than those normally taken by a pregnant woman when travelling, need be observed, apart from those recommended for all travellers by air.

KENNETH G. BERGIN, M.D.
*Assistant Director Medical Services,
British Overseas Airways Corporation.*

Prophylaxis of the Common Cold

QUERY.—I should be grateful if you could tell me which is the best preventive for winter colds. Are the sulphonamides or penicillin of any value?

REPLY.—No effective prophylactic against winter colds is known. *Bacterial vaccines* of various sorts have had a wide vogue, but no statistical evidence of their value has ever been obtained in a satisfactorily controlled investigation. Ultra-violet light and vitamins, especially A and D, have also been employed, but with these again, although some workers have claimed good results especially with ultra-violet light, no statistically satisfactory evidence of their value has been obtained.

With regard to the *sulphonamides*, the experience of the United States armed forces, especially the Navy, is of interest. Preliminary reports of the use of sulphonamides, in dosages of 0.5 to 1.0 gm. daily, in the prophylaxis of epidemic respiratory infections showed a statistically significant diminution in hæmolytic streptococcal infections, but further experience showed that the organisms became sulphonamide-fast, and in many centres even worse epidemics then occurred than had been observed before the use of sulphonamide prophylaxis. The diminution in respiratory infections in the earlier part of this investigation applied only to streptococcal infections and not to the common cold, which is generally accepted as a virus infection.

No information is available about the prophylactic value of *penicillin* against respiratory infections in general. *A priori* it might be expected that penicillin would be effective only against infections by streptococci and other penicillin-sensitive bacteria; there has been no evidence that penicillin has any effect against virus infections. The only practicable way of using penicillin prophylactically would be in the form of lozenges. It is conceivable that these might be of value in the presence of an epidemic of streptococcal infections, but it is improbable that they would diminish the liability to virus infections.

In any patient who seems to be unduly liable to the common cold the question of an allergic background or of chronic infections of the nasal sinuses should be investigated.

J. G. SCADDING, M.D., F.R.C.P.

The Treatment of Black Hairy Tongue

QUERY.—In November 1945, a lady farmer noticed that her tongue was covered with a black fur especially marked over the posterior third. In July 1946, a swab was taken and the

pathologist reported the following:—"*Direct smear*: a few pus cells and epithelial cells present; crowded with organisms including monilia and other yeasts. Culture: a yeast-like organism is obtained, corresponding to *Cryptococcus linguæ pilosæ*; the organisms of melanoglossia". It is fully realized that this is of no clinical significance but from a social point of view it is a distinct drawback. Could advice be given as to some form of treatment?

REPLY.—Since black hairy tongue is probably an inflammatory state brought about by some form of irritant, it is important to eliminate anything of the nature, e.g. oral sepsis, excessive use of tobacco, astringent mouthwashes. It is usually extremely resistant to all forms of treatment, but is apt to undergo spontaneous recession and has a marked tendency to recurrence. The condition is said to be of the nature of a metaplasia of the epithelium leading to a keratinization of the tips of the filiform papillæ and therefore a keratin solvent is helpful. The papillæ may be shaved down with a razor blade, the tongue dried and application made of a 10 per cent. solution of salicylic acid in equal parts of glycerin and alcohol, followed by hydrogen peroxide and a saline mouthwash. As an alternative a single application of 50 per cent. trichloracetic acid may succeed. An alkaline mouthwash, such as liquor potassæ, has been reported successful, as also has the application of mild doses of X-rays and radium.

A. L. SPENCER-PAYNE, M.R.C.S., L.R.C.P., L.D.S.

Magnesium Sulphate in Toxæmia of Pregnancy

QUERY.—I was interested in Dr. Rickford's article on the toxæmia of pregnancy in the August number of *The Practitioner*, but was surprised to see no mention whatsoever of the use of magnesium sulphate intramuscularly, since I have used this in treatment of eclampsia in village homes in India, where everything is adverse to treatment, so far as surroundings are concerned. I have only lost one patient, who was dying when I was called, and recurrence of fits occurred in only one patient. The number of cases is small, being about eight, but previously I lost every case. In India, patients have usually been having fits for some time before we get to them. I should be interested to know if Dr. Rickford has used magnesium sulphate intramuscularly in the treatment of eclampsia and what his results have been.

REPLY.—Shogaroff and Dairdovitch (1937) report two hundred cases of eclampsia treated with subcutaneous magnesium sulphate with the excellent result of only six deaths (3 per cent.). A dose of 6 gm. is given in a 15 per cent.

solution and the same dose repeated after three-and-a-half hours if there have been further fits (for details see the original article). This drug has also been given intravenously with good results but its use by this route is considered to be too dangerous. Intramuscular magnesium sulphate, in 50 per cent. solution, displaced the subcutaneous method, as the latter was inclined to produce abscess formation. Greene (1945) has recently ceased to use this drug and is of the opinion that his results are probably as good without it. The magnesium ion has a marked sedative effect on the nervous system but it is not without danger. An antidote (10 gm. of a 5 per cent. solution of calcium chloride) should always be at hand for intravenous use.

References

Greene, G. A. (1945): *Amer. J. Obst. Gynec.*, 50, 427.
Shogaroff, W., and Dairdovitch, O. (1937): *J. Obst. Gynæc.*, 44, 289.

BRAITHWAITE RICKFORD, M.D., F.R.C.S., F.R.C.O.G.

Hæmophilia and Heredity

QUERY.—What Mendelian factors are concerned in the transmission of hæmophilia? If a hæmophiliac marries a normal woman, what proportion of his daughters will be carriers? Will any of his sons be hæmophiliacs? In practice, if a negative family history is obtained in the near relatives, e.g. parents, grandparents and great-grandparents, and if the case is otherwise typically one of hæmophilia (and the plasma fibrinogen is within normal limits), is the diagnosis still hæmophilia, and if so how can this be explained?

REPLY.—Hæmophilia is an example of sex-linked inheritance of the recessive type. It is due to a gene carried upon the unpaired portion of the X chromosome. If a hæmophilic man has children by a normal woman, all his sons will be normal and all his daughters will be carriers. No family history of the disease is obtained in approximately 15 per cent. of hæmophiliacs. One possible explanation of this is that the recessive gene has been handed on undetected through one or two generations, for with the usual transmission through the female only half of the sons are hæmophilic and half of the daughters carriers. The odds against this happening for more than two or three generations are high and it is therefore believed that the majority of examples of sporadic hæmophilia are new mutant forms of the disease. This leads to the rather Calvinistic doctrine that as hæmophilia dies out by lack of viability of the affected stock, so it is steadily replaced by mutations.

PROFESSOR L. J. WITTS, M.D., F.R.C.P.

PRACTICAL NOTES

Typhoid Vaccine in the Treatment of Ulcerative Colitis

AT the Lahey Clinic, Boston, Mass., the criteria for the selection of patients with ulcerative colitis for treatment with typhoid vaccine are, that the disease process should be in the chronic phase and that the patients are afebrile, free from concomitant disease and have adequate cardiac, renal and hepatic reserves (S. A. Wilkinson and F. H. Smith, *Gastroenterology*, March 1946, 6, 171). The method of treatment is as follows :—A temperature of 102 to 103° F. (38.8 to 39.3° C.) has been found to yield the best results. The vaccine is given intravenously and the initial dose varies from 3 to 15 million organisms, smaller doses being given when there is a history of allergy or asthma. Injections are given on alternate days, and a "course" consists of ten injections. Subsequent to the initial dose, each dose consists of a 50 per cent. increase on the previous one. Should too severe a reaction result from the initial injection, the second one should be only a third of the original one and this smaller dose should be maintained for several injections. The typical reaction consists of a chill coming on one to three hours after the injection and a rise of temperature to 102 or 103° F. (38.8 to 39.3° C.). The pyrexia persists for two to four hours. Headache is a common symptom, and the general state of malaise persists for about twelve hours, although it may occasionally last for thirty-six hours. If the response to the first course is satisfactory it should be repeated at fortnightly intervals, and later at monthly intervals, the dosage being one-third of that given in the original course. These subsequent courses can be given in the patient's own home. Of forty patients receiving this treatment, twenty-seven (68 per cent.) were greatly improved or completely relieved, ten (25 per cent.) were slightly to moderately improved, and three (7 per cent.) showed no improvement. In the "one-and-a-half year average follow-up" the corresponding figures were:—50 per cent. remained greatly improved or completely relieved, 28 per cent. were slightly to moderately improved, 10 per cent. showed no improvement, 7 per cent. required ileostomy, and 5 per cent. were dead. In a control group of thirty-two patients receiving some other form of medical treatment, a follow-up after an average of two-and-a-half years gave the following results:—34 per cent. greatly improved or cured, 41 per cent. slight or moderately improved, 6 per cent. unimproved; 19 per cent. were not followed up or were known to have died. The status of this form of treatment is summed up as follows:—"In the afebrile, fairly well-nourished, younger group, those who can tolerate some constitutional insult in addition to their already existing disease, typhoid therapy offers a means of restoring to active life a reasonably high percentage, which in this series was more than half of those treated."

The Use of Demerol in Labour

DEMEROL (ethylmethylphenyl piperidine carboxylate) is a synthetic coal tar product with atropine-, morphine- and papaverine-like properties. At the Toronto General Hospital, from February to June 1945, it was used as a routine on public ward patients for the relief of pain during labour. The results are recorded by W. D. Flatt (*Canadian Medical Association Journal*, July 1946, 55, 43). The method of administration adopted in the reported series was:—demerol 100 mgm., hyoscine 1/150 grain (0.43 mgm.), with or without sodium amytal, 3 grains (0.2 gm.); repeat demerol 100 mgm. in one hour, then demerol, 100 mgm., and hyoscine, 1/400 grain (0.16 mgm.), three-hourly, or when necessary. The analgesic effect of demerol is enhanced by hyoscine and sodium amytal, but it must be borne in mind that larger doses of these drugs than those advocated may predispose the infant to anoxæmia. Demerol is given either intramuscularly or intravenously; if by the latter route, it should be diluted with 8 c.cm. of normal saline and given slowly over a period of two minutes. The duration of the effects of the drug by both routes of administration is from one to three hours; with intravenous administration there is immediate relief from pain, and when given intramuscularly the relief occurs within five to fifteen minutes. In many cases in the series no anæsthetic was necessary for delivery, and it is stated that if anæsthetic agents are not available or inhalation is contraindicated, frequent administration of demerol may suffice. Attention has been drawn, however, to the risk of addiction with the use of demerol (*Journal of the American Medical Association*, 1946, 131, 937, and 132, 26, 43), and it is well that its habit-forming properties should be borne in mind.

Penicillin in the Treatment of Infected Tooth Sockets

THE local application of penicillin to infected tooth sockets in thirty-five cases of severe pain after extractions is recorded by F. Driak (*Wiener Klinische Wochenschrift*, August 9, 1946, 58, 455). After the affected areas had been

wiped with sterile gauze or cotton swabs the sockets were rinsed with sterilized distilled water or physiological saline solution, the alveoli dried with wool or gauze swabs and the area kept dry by means of cotton wool rolls, as used for fillings. For each application a fresh penicillin solution, made from one tablet of 9000 Oxford units in ½ c.cm. of distilled water, was used, strips of gauze being soaked therein and placed in the affected tooth sockets up to two-thirds of their height. Excess of fluid was removed with a dry swab and the sockets filled with small gauze swabs soaked in mastisol or cohesan (an adhesive substance containing acetone and cellulose). In this way the sockets were protected from infection and the local action of the penicillin assured. The penicillin can be applied in the form of a powder by crushing the tablets, but the distribution by this method is not so good. After two to three days the packing and penicillin gauze strips are removed. In most cases one dressing was sufficient; in two cases a second application was necessary, and in four there was no benefit from the treatment. In the thirty-one cases in which the treatment was successful, all the patients reported a feeling of burning and throbbing in the affected sockets six to eight hours after the application of the penicillin, with temporary increase in the pain and then sudden disappearance without recurrence. Seven cases of extraction of lower wisdom teeth and three of upper wisdom teeth were included in the series. In the majority of cases the sockets were clean on removal of the penicillin dressings and healing was rapid. In the four cases regarded as failures the pain did not disappear until eight to eleven days after treatment.

The Surgical Treatment of Patent Ductus Arteriosus

It is well known that the ductus arteriosus, which is patent during the early days of life, remains so in some children for months, years, or even throughout life. This results in the pulmonary artery being fed from two sources and thus imposes an additional load on the heart with the risk of fatal complications, such as bacterial endocarditis and congestive heart failure. These facts are pointed out by A. R. Gilchrist (*Edinburgh Medical Journal*, July 1946, 53, 346) who reports the results of observations on forty patients of ages ranging from four to fifty-one years of age. In order to avoid the risk of later complications, ligation of the ductus should be carried out in all children so affected between the ages of seven and ten years; over the age of ten the operation should only be performed if the patient shows some slight

disability, and over the age of twenty ligation is justified only if heart failure threatens or if symptoms increase in gravity. When the ductus is infected, operation should be carried out at the first opportunity: of four patients in the series so treated, three died and one, a child of six, made a brilliant and prompt recovery. In the remaining thirty-six patients of the series the ductus was non-infected: operation was carried out in sixteen, with satisfactory results in thirteen, failure in one, and two patients died after the operation. Mention is made of the improved operative technique advocated by Touroff, consisting of subadventitial dissection on the aortic arch, which renders recanalization less likely. W. Mercer (*Ibid.*, 355) discusses this method in detail; he has used it for dissection at the aortic end of the ductus in a small series of infected cases in which dramatic results were obtained, the blood stream being free of organisms within a few minutes of ligation and the temperature normal in a short while. Mention is also made of the recent American method of ligation at either end of the ductus and division between the ligatures, which method was used by Tudor Edwards in a case in which hæmorrhage had occurred.

A New Reagent for Detecting Albumin in the Urine

As a result of their experience with 10,000 specimens of urine, A. Bernhard and Y. Scher (*American Journal of Clinical Pathology*, May 1946, 16, 96) recommend the use of a new reagent which will demonstrate the presence of albumin in a dilution of 1:150,000. The reagent is prepared by mixing a 20 per cent. aqueous solution of sulphosalicylic acid with an equal volume of methanol; the solution is then filtered. The test is carried out by adding 6 to 8 drops of the reagent to 5 c.cm. of urine. The reagent forms a layer on top of the urine and the presence of albumin is indicated by a white flocculation which appears within five minutes and does not change after an hour. The amount of flocculation depends upon the amount of albumin present. Clouding of the urine due to phosphates is cleared by the reagent; although this clearing does not occur in the case of cloudiness due to urates, there is no difficulty in detecting the flocculation in such cases.

Procaine in the Treatment of Acute Sprains of the Ankle

"Excellent and permanent results" are recorded by C. W. McLaughlin, Jun. (*Surgery*, August 1946, 20, 280) in 86 per cent. of cases, from the use of procaine infiltration in the

treatment of acute sprains of the ankle in a series of 65 patients, provided the treatment was given within twenty-four hours after the occurrence of the injury. A careful radiological examination is an essential preliminary, to exclude the presence of two contraindications to this form of treatment: the presence of bony injury, and extensive ligamentous damage, particularly of the calcaneo-fibular ligament. The technique of injection consists first of all in localization of the points of maximum tenderness. The skin having then been prepared with soap and water and an antiseptic solution, 10 to 20 c.cm. of 1 per cent. procaine, without adrenaline, is injected into each tender area. The site of injection is then gently massaged to diffuse the procaine, and the foot is moved in all directions to demonstrate any residual discomfort. Unless this procedure demonstrates complete relief from pain, satisfactory results will not be obtained. Each injection site is covered with a patch dressing, and the shoes are put on tightly laced. The patient is then observed while he carries out exercises to place the ankle in a variety of positions. If the injection has been satisfactory the patient experiences "immediate and complete relief of pain". He is then advised to remain active for several hours, and is re-examined in twenty-four hours. Should pain have recurred by this time the tender spots are again injected. Eight patients in this series required a second injection on account of recurrence of pain, and of these, excellent results were obtained in four, and a fair result in one. Re-examination of the remaining three patients showed that one had a fissure fracture of the os calcis, one had a fracture of the posterior astragalus and one had an extensive ligamentous tear.

The Masking of Syphilis by Penicillin

ONE of the recognized risks of the treatment of gonorrhœa with penicillin is that such treatment may mask the presence of syphilis. In a series of about 1000 patients with early syphilis, S. Fromer et al. (Journal of Venereal Disease Information, July 1946, 27, 174) found 66 who had had penicillin therapy for gonorrhœa within the incubation period of syphilis; none of these patients gave a history of a penile sore at the time of the first course of treatment. Of these 66 patients, 18 gave a history of a chilly sensation and/or fever accompanying the treatment. This is considered to have been a Herxheimer reaction, which is said to occur in about 90 per cent. of all cases of early syphilis during treatment with penicillin. As such febrile reactions are extremely rare in the penicillin treatment of gonorrhœa (an incidence of 2 or 3 per 2000 patients is recorded), the suggestion

is made that "the occurrence of chills or fever accompanying penicillin therapy for gonorrhœa not obviously complicated by syphilis is strong presumptive evidence of the coexistence of syphilis. Although there are exceptions to the rule, it appears to be a safe precaution to subject a patient displaying a febrile reaction to penicillin to close scrutiny, clinical and serologic, for a period of four months following therapy. Within that period additional evidence of an oncoming syphilis may be expected to develop".

Chewing Gum and Gastric Acidity

THE effect of chewing gum, composed of chicle and oil of peppermint, upon gastric acidity in twelve healthy individuals has been investigated by C. S. Smith et al. (American Journal of Digestive Diseases, August 1946, 13, 245). Their technique was to chew 2 gm. of chewing gum for five minutes following the administration of a standard test meal of crackers and water. Total and free acid were then estimated on specimens of gastric juice withdrawn at fifteen-minute intervals. As compared with the result obtained in the same individuals when gastric analysis was carried out when no chewing gum was used, the main effect of chewing gum was a lowering of total acidity: this occurred in eleven subjects, and in the remaining one it was only raised 0.6 degree. There was no constant effect upon the time required for the attainment of maximum acidity. The effect upon free acidity was inconstant: in six subjects the average maximum free acidity was increased, whereas in six it was decreased. During the first half-hour both total and free acidity were depressed in nine of the individuals investigated. After half-an-hour the free acid did not appear to be influenced by gum chewing, but the depressant effect upon total acidity was still found at the end of an hour in eight subjects.

Tannic Acid Barium Enemas

THE addition of one level tablespoonful of powdered tannic acid to each 2 quarts of barium and water mixture has proved so satisfactory, according to Col. J. B. Hamilton of the U.S. Army Medical Corps (American Journal of Rœntgenology, July 1946, 56, 101) that it has been adopted as a routine measure in all barium enema examinations carried out at the army hospital to which he is attached. The advantage of this addition is that it results in better mucosal patterns on the evacuation films. No complaints of unpleasant after-effects have been encountered. In preparing the patient for examination, castor oil or compound liquorice powder is given in addition to a tap water enema, unless contraindicated.

wiped with sterile gauze or cotton swabs the sockets were rinsed with sterilized distilled water or physiological saline solution, the alveoli dried with wool or gauze swabs and the area kept dry by means of cotton wool rolls, as used for fillings. For each application a fresh penicillin solution, made from one tablet of 9000 Oxford units in $\frac{1}{2}$ c.cm. of distilled water, was used, strips of gauze being soaked therein and placed in the affected tooth sockets up to two-thirds of their height. Excess of fluid was removed with a dry swab and the sockets filled with small gauze swabs soaked in mastisol or cohesan (an adhesive substance containing acetone and cellulose). In this way the sockets were protected from infection and the local action of the penicillin assured. The penicillin can be applied in the form of a powder by crushing the tablets, but the distribution by this method is not so good. After two to three days the packing and penicillin gauze strips are removed. In most cases one dressing was sufficient; in two cases a second application was necessary, and in four there was no benefit from the treatment. In the thirty-one cases in which the treatment was successful, all the patients reported a feeling of burning and throbbing in the affected sockets six to eight hours after the application of the penicillin, with temporary increase in the pain and then sudden disappearance without recurrence. Seven cases of extraction of lower wisdom teeth and three of upper wisdom teeth were included in the series. In the majority of cases the sockets were clean on removal of the penicillin dressings and healing was rapid. In the four cases regarded as failures the pain did not disappear until eight to eleven days after treatment.

The Surgical Treatment of Patent Ductus Arteriosus

IT is well known that the ductus arteriosus, which is patent during the early days of life, remains so in some children for months, years, or even throughout life. This results in the pulmonary artery being fed from two sources and thus imposes an additional load on the heart with the risk of fatal complications, such as bacterial endocarditis and congestive heart failure. These facts are pointed out by A. R. Gilchrist (*Edinburgh Medical Journal*, July 1946, 53, 346) who reports the results of observations on forty patients of ages ranging from four to fifty-one years of age. In order to avoid the risk of later complications, ligation of the ductus should be carried out in all children so affected between the ages of seven and ten years; over the age of ten the operation should only be performed if the patient shows some slight

disability, and over the age of twenty ligation is justified only if heart failure threatens or if symptoms increase in gravity. When the ductus is infected, operation should be carried out at the first opportunity: of four patients in the series so treated, three died and one, a child of six, made a brilliant and prompt recovery. In the remaining thirty-six patients of the series the ductus was non-infected: operation was carried out in sixteen, with satisfactory results in thirteen, failure in one, and two patients died after the operation. Mention is made of the improved operative technique advocated by Touroff, consisting of subadventitial dissection on the aortic arch, which renders recanalization less likely. W. Mercer (*Ibid.*, 355) discusses this method in detail; he has used it for dissection at the aortic end of the ductus in a small series of infected cases in which dramatic results were obtained, the blood stream being free of organisms within a few minutes of ligation and the temperature normal in a short while. Mention is also made of the recent American method of ligation at either end of the ductus and division between the ligatures, which method was used by Tudor Edwards in a case in which hæmorrhage had occurred.

A New Reagent for Detecting Albumin in the Urine

As a result of their experience with 10,000 specimens of urine, A. Bernhard and Y. Scher (*American Journal of Clinical Pathology*, May 1946, 16, 96) recommend the use of a new reagent which will demonstrate the presence of albumin in a dilution of 1:150,000. The reagent is prepared by mixing a 20 per cent. aqueous solution of sulphosalicylic acid with an equal volume of methanol; the solution is then filtered. The test is carried out by adding 6 to 8 drops of the reagent to 5 c.cm. of urine. The reagent forms a layer on top of the urine and the presence of albumin is indicated by a white flocculation which appears within five minutes and does not change after an hour. The amount of flocculation depends upon the amount of albumin present. Clouding of the urine due to phosphates is cleared by the reagent; although this clearing does not occur in the case of cloudiness due to urates, there is no difficulty in detecting the flocculation in such cases.

Procaine in the Treatment of Acute Sprains of the Ankle

"EXCELLENT and permanent results" are recorded by C. W. McLaughlin, Jun. (*Surgery*, August 1946, 20, 280) in 86 per cent. of cases, from the use of procaine infiltration in the

son, Dean Swift, George III, Byron and many others. For the medical man who is also a literary dilettante, the book will be a source of perpetual pleasure.

Fundamentals of Immunology. BY W. C. BOYD, PH.D. London: Staples Press, Ltd., 1946. Pp. xiv and 446. Figures 42. Price 33s.

WITH its theories masked by an obscure terminology, and practice shrouded in columns of statistics, immunology has tended to exchange the attention of the medical world at large for that of a small band of initiates. This mutually unfortunate divorce is, no doubt, a reaction to the somewhat exaggerated hopes engendered in the early years of the century by such successes as the prophylactic use of Sir Almroth Wright's T.A.B. vaccine. For those who wish to renew their acquaintance with what is, after all, one of the basic sciences upon which modern medical practice depends, this book provides a readable account of its present status and practical applications. Parts may seem heavy going but a well-designed index makes it into a more than usually helpful book of reference. This edition is a reprint of one published in the U.S.A. in 1942, which explains the absence of more complete information on the subject of the Rhesus factor in the chapter on blood groups. The advice on the occurrence of shock following the administration of serum is misleading. No test will foretell its occurrence and a syringe of adrenaline should always be at hand when serum is given; more than usual caution must be employed when it is necessary to administer serum to those who suffer from asthma. The printing, illustrations and lay-out are good, but future editions would be improved if the chapter on practical procedures was divided into those used in the laboratory and those at the bedside.

Psychology of Women: I. Girlhood. BY HELENE DEUTSCH, M.D. London: Research Books Ltd., 1946. Pp. xi and 312. Price 21s.

ALTHOUGH this book is essentially for the specialist it contains much information of practical value for the general medical reader, avoiding to a much greater extent than usual the obscurities which the overuse of a specialized vocabulary so often involves. The writer is a disciple of Freud but holds her own opinions throughout—for example, she draws constant attention to the differences between male and female development even in pre-pubertal years, a point so often overlooked in this type of literature. The different stages of feminine development are dealt with in an expert manner and clearly from much personal clinical experience. The chapters on the pre-pubertal and menopausal periods particularly, contain much that is of value. Later chapters on the more special and the abnormal developments of feminine psychology are of much interest, although it might perhaps be said that the structural and constitutional aspects of the author's cases are not taken sufficiently into account. This book is certainly worth reading.

The British Encyclopædia of Medical Practice: Medical Progress and Cumulative Supplement, 1946. Edited by the RT. HON. LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P. London: Butterworth & Co. (Publishers) Ltd., 1946. Pp. v, 458 and 40 and 267. Price 37s. 6d.

ONE of the most welcome inclusions in Medical Progress 1946, is a chapter on penicillin by Sir Howard Florey, in which he gives a full survey of the knowledge and uses of penicillin up to date, with methods of administration, dosage and the value of penicillin in the treatment of different diseases. The chapter on mental diseases, by the late R. D. Gillespie, will be read with interest and deep regret as the last that will come from his pen. In the introduction the Editor in Chief pays a graceful tribute to the late Sir Humphry Rolleston and his irreplaceable work in the field of medical literature.

NEW EDITIONS

IN the preparation of the fifth edition of *The Nervous Child,* by H. C. Cameron, M.D., F.R.C.P. (Oxford University Press, 10s. 6d.) rewriting has not been undertaken, but the author has added several new sections dealing respectively with umbilical colic, night terrors, vomiting in infancy and excessive depth of sleep in enuresis. The prevention of nervous phenomena in children is a subject of general interest to practitioners, who will find in this little book much practical advice which does not impinge on the nowadays somewhat overstressed field of psychiatry.

Medical Emergencies, by CHARLES NEWMAN, M.D., F.R.C.P., in its third edition (J. & A. Churchill Ltd., 10s. 6d.) has been subjected to a number of alterations, and sections on the sulphonamides and penicillin have been added. The author's method of a brief outline of the symptoms followed by instructions for treatment makes this book a valuable addition to the everyday library of the practitioner.

REVIEWS OF BOOKS

The Peripheral Circulation in Health and Disease. By ROBERT L. RICHARDS, M.D. Foreword by PROFESSOR J. R. LEARMONTH, C.B.E., CH.M., F.R.C.S.ED. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. xii and 153. Figures 104. Price 21s.

THIS handsomely produced monograph is a useful contribution to a highly specialized branch of medicine. Based upon an investigation carried out in Edinburgh, under the direction of Professor Learmonth, it provides an excellent example of how clinical investigation should be carried out. Introductory chapters are devoted to the anatomy and physiology of the peripheral vasomotor system and methods of study of the system. These are followed by chapters on occlusive vascular disease, the Raynaud phenomenon, peripheral nerve injuries and the immersion foot syndrome. An extensive bibliography adds considerably to the value of the work. In face of this carefully accumulated wealth of information it is a humbling thought that over eighty years have passed since Raynaud first described the condition to which his name is attached; for to-day, in spite of all the careful work on the subject that has been done during two world wars, "clinical science" has added many stones to the edifice, but it has failed to provide the coping stone that will complete the edifice. Indeed, the more data that issue from the laboratory (clinical or physiological), the more complex does the problem appear. As an attempt not merely to add to the sum total of factual data, but to merge the known facts into a recognized pattern, this monograph will be welcomed by all who have an interest in this intriguing problem of the peripheral circulation and its disorders.

Ancient Anodynes. By E. S. ELLIS, M.R.C.S., F.R.A.I. With Foreword by T. K. PENNIMAN, M.A. London: William Heinemann (Medical Books) Ltd., 1946. Pp. 187. Price 21s.

THIS book, appropriately appearing in the centenary year of ether, will be of interest to both medical men and anthropologists. Using the term "anæsthesia" in a wide sense, the author has dealt with the many methods which have been used throughout the ages to assuage pain. This covers a vast field from primitive man down to the introduction of chloroform as an anæsthetic. As is inevitable in dealing with ancient usages, considerable space is devoted to the use of inebriants, until quite recent times one of the most widely used methods of relieving pain. An amazing amount of information is packed into these pages, and this, combined with the rather stilted style in which the book is written, does not make for easy reading. As it is primarily a reference book, however, this criticism does not detract from its essential value. On the other hand, it is a pity that a fuller index has not been provided. The scope of the book is well summed up in the foreword by the Curator of the Pitt Rivers Museum in the University of Oxford: "Here can be found a vast number of ways by which humanity has attempted to assuage its ills ... Dr. Ellis, with his medical knowledge, has been able to assess their value, medically and psychologically".

How a Baby Grows. By ARNOLD GESELL, M.D. London: Hamish Hamilton, Medical Books, 1946. Pp. vii and 78. Price 10s. 6d.

THIS is a profusely illustrated book, with a series of short commentaries by the famous director of the Yale Clinic of Child Development. The photographs are selected from the cinematographic records and "still" pictures prepared over a seven-years period for the *Atlas of Infant Behaviour*. The present volume is obviously more intended for parents than for the scientific student of infant and child development, but it should prove a useful reference work for all those concerned with children. The photographs are beautifully reproduced and skilfully arranged, covering various aspects of the baby and child during the first five years of life.

Analecta Psychiatrica. By J. R. WHITWELL, M.B. London: H. K. Lewis & Co., Ltd., 1946. Pp. 160. Price 16s.

THE author of this book, a former superintendent of a mental hospital, is the honorary librarian of the Royal Medico-Psychological Association. "This collection of psychiatric miscellanies", as Dr. Whitwell describes it in his preface, makes fascinating reading. Taking the whole range of literature from Plato to Wordsworth as his field, he has amassed a wealth of sayings of the great figures of literature concerning mental disorders. These quotations are divided into sections dealing with forms of mental disorder, suicide, causes of mental disorder, treatment, and pathology. The concluding section deals with "some interesting cases" of insanity, including Samuel John-

son, Dean Swift, George III, Byron and many others. For the medical man who is also a literary dilettante, the book will be a source of perpetual pleasure.

Fundamentals of Immunology. By W. C. Boyd, ph.d. London: Staples Press, Ltd., 1946. Pp. xiv and 446. Figures 42. Price 33s.

With its theories masked by an obscure terminology, and practice shrouded in columns of statistics, immunology has tended to exchange the attention of the medical world at large for that of a small band of initiates. This mutually unfortunate divorce is, no doubt, a reaction to the somewhat exaggerated hopes engendered in the early years of the century by such successes as the prophylactic use of Sir Almroth Wright's T.A.B. vaccine. For those who wish to renew their acquaintance with what is, after all, one of the basic sciences upon which modern medical practice depends, this book provides a readable account of its present status and practical applications. Parts may seem heavy going but a well-designed index makes it into a more than usually helpful book of reference. This edition is a reprint of one published in the U.S.A. in 1942, which explains the absence of more complete information on the subject of the Rhesus factor in the chapter on blood groups. The advice on the occurrence of shock following the administration of serum is misleading. No test will foretell its occurrence and a syringe of adrenaline should always be at hand when serum is given; more than usual caution must be employed when it is necessary to administer serum to those who suffer from asthma. The printing, illustrations and lay-out are good, but future editions would be improved if the chapter on practical procedures was divided into those used in the laboratory and those at the bedside.

Psychology of Women: I. Girlhood. By Helene Deutsch, m.d. London: Research Books Ltd., 1946. Pp. xi and 312. Price 21s.

Although this book is essentially for the specialist it contains much information of practical value for the general medical reader, avoiding to a much greater extent than usual the obscurities which the overuse of a specialized vocabulary so often involves. The writer is a disciple of Freud but holds her own opinions throughout—for example, she draws constant attention to the differences between male and female development even in pre-pubertal years, a point so often overlooked in this type of

literature. The different stages of feminine development are dealt with in an expert manner and clearly from much personal clinical experience. The chapters on the pre-pubertal and menopausal periods particularly, contain much that is of value. Later chapters on the more special and the abnormal developments of feminine psychology are of much interest, although it might perhaps be said that the structural and constitutional aspects of the author's cases are not taken sufficiently into account. This book is certainly worth reading.

The British Encyclopædia of Medical Practice: Medical Progress and Cumulative Supplement, 1946. Edited by the Rt. Hon. Lord Horder, g.c.v.o., m.d., b.sc., f.r.c.p. London: Butterworth & Co. (Publishers) Ltd., 1946. Pp. v, 458 and 40 and 267. Price 37s. 6d.

One of the most welcome inclusions in Medical Progress 1946, is a chapter on penicillin by Sir Howard Florey, in which he gives a full survey of the knowledge and uses of penicillin up to date, with methods of administration, dosage and the value of penicillin in the treatment of different diseases. The chapter on mental diseases, by the late R. D. Gillespie, will be read with interest and deep regret as the last that will come from his pen. In the introduction the Editor in Chief pays a graceful tribute to the late Sir Humphry Rolleston and his irreplaceable work in the field of medical literature.

NEW EDITIONS

In the preparation of the fifth edition of *The Nervous Child,* by H. C. Cameron, m.d., f.r.c.p. (Oxford University Press, 10s. 6d.) rewriting has not been undertaken, but the author has added several new sections dealing respectively with umbilical colic, night terrors, vomiting in infancy and excessive depth of sleep in enuresis. The prevention of nervous phenomena in children is a subject of general interest to practitioners, who will find in this little book much practical advice which does not impinge on the nowadays somewhat overstressed field of psychiatry.

Medical Emergencies, by Charles Newman, m.d., f.r.c.p., in its third edition (J. & A. Churchill Ltd., 10s. 6d.) has been subjected to a number of alterations, and sections on the sulphonamides and penicillin have been added. The author's method of a brief outline of the symptoms followed by instructions for treatment makes this book a valuable addition to the everyday library of the practitioner.

REVIEWS OF BOOKS

The Peripheral Circulation in Health and Disease. BY ROBERT L. RICHARDS, M.D. Foreword by PROFESSOR J. R. LEARMONTH, C.B.E., CH.M., F.R.C.S.ED. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. xii and 153. Figures 104. Price 21s.

THIS handsomely produced monograph is a useful contribution to a highly specialized branch of medicine. Based upon an investigation carried out in Edinburgh, under the direction of Professor Learmonth, it provides an excellent example of how clinical investigation should be carried out. Introductory chapters are devoted to the anatomy and physiology of the peripheral vasomotor system and methods of study of the system. These are followed by chapters on occlusive vascular disease, the Raynaud phenomenon, peripheral nerve injuries and the immersion foot syndrome. An extensive bibliography adds considerably to the value of the work. In face of this carefully accumulated wealth of information it is a humbling thought that over eighty years have passed since Raynaud first described the condition to which his name is attached; for to-day, in spite of all the careful work on the subject that has been done during two world wars, "clinical science" has added many stones to the edifice, but it has failed to provide the coping stone that will complete the edifice. Indeed, the more data that issue from the laboratory (clinical or physiological), the more complex does the problem appear. As an attempt not merely to add to the sum total of factual data, but to merge the known facts into a recognized pattern, this monograph will be welcomed by all who have an interest in this intriguing problem of the peripheral circulation and its disorders.

Ancient Anodynes. By E. S. ELLIS, M.R.C.S., F.R.A.I. With Foreword by T. K. PENNIMAN, M.A. London: William Heinemann (Medical Books) Ltd., 1946. Pp. 187. Price 21s.

THIS book, appropriately appearing in the centenary year of ether, will be of interest to both medical men and anthropologists. Using the term "anæsthesia" in a wide sense, the author has dealt with the many methods which have been used throughout the ages to assuage pain. This covers a vast field from primitive man down to the introduction of chloroform as an anæsthetic. As is inevitable in dealing with ancient usages, considerable space is devoted to the use of inebriants, until quite recent times one of the most widely used methods of relieving pain. An amazing amount of information is packed into these pages, and this, combined with the rather stilted style in which the book is written, does not make for easy reading. As it is primarily a reference book, however, this criticism does not detract from its essential value. On the other hand, it is a pity that a fuller index has not been provided. The scope of the book is well summed up in the foreword by the Curator of the Pitt Rivers Museum in the University of Oxford: "Here can be found a vast number of ways by which humanity has attempted to assuage its ills . . . Dr. Ellis, with his medical knowledge, has been able to assess their value, medically and psychologically".

How a Baby Grows. BY ARNOLD GESELL, M.D. London: Hamish Hamilton, Medical Books, 1946. Pp. vii and 78. Price 10s. 6d.

THIS is a profusely illustrated book, with a series of short commentaries by the famous director of the Yale Clinic of Child Development. The photographs are selected from the cinematographic records and "still" pictures prepared over a seven-years period for the *Atlas of Infant Behaviour.* The present volume is obviously more intended for parents than for the scientific student of infant and child development, but it should prove a useful reference work for all those concerned with children. The photographs are beautifully reproduced and skilfully arranged, covering various aspects of the baby and child during the first five years of life.

Analecta Psychiatrica. By J. R. WHITWELL, M.B. London: H. K. Lewis & Co., Ltd., 1946. Pp. 160. Price 16s.

THE author of this book, a former superintendent of a mental hospital, is the honorary librarian of the Royal Medico-Psychological Association. "This collection of psychiatric miscellanies", as Dr. Whitwell describes it in his preface, makes fascinating reading. Taking the whole range of literature from Plato to Wordsworth as his field, he has amassed a wealth of sayings of the great figures of literature concerning mental disorders. These quotations are divided into sections dealing with forms of mental disorder, suicide, causes of mental disorder, treatment, and pathology. The concluding section deals with "some interesting cases" of insanity, including Samuel John-

son, Dean Swift, George III, Byron and many others. For the medical man who is also a literary dilettante, the book will be a source of perpetual pleasure.

Fundamentals of Immunology. BY W. C. BOYD, PH.D. London: Staples Press, Ltd., 1946. Pp. xiv and 446. Figures 42. Price 33s.

WITH its theories masked by an obscure terminology, and practice shrouded in columns of statistics, immunology has tended to exchange the attention of the medical world at large for that of a small band of initiates. This mutually unfortunate divorce is, no doubt, a reaction to the somewhat exaggerated hopes engendered in the early years of the century by such successes as the prophylactic use of Sir Almroth Wright's T.A.B. vaccine. For those who wish to renew their acquaintance with what is, after all, one of the basic sciences upon which modern medical practice depends, this book provides a readable account of its present status and practical applications. Parts may seem heavy going but a well-designed index makes it into a more than usually helpful book of reference. This edition is a reprint of one published in the U.S.A. in 1942, which explains the absence of more complete information on the subject of the Rhesus factor in the chapter on blood groups. The advice on the occurrence of shock following the administration of serum is misleading. No test will foretell its occurrence and a syringe of adrenaline should always be at hand when serum is given; more than usual caution must be employed when it is necessary to administer serum to those who suffer from asthma. The printing, illustrations and lay-out are good, but future editions would be improved if the chapter on practical procedures was divided into those used in the laboratory and those at the bedside.

Psychology of Women: I. Girlhood. BY HELENE DEUTSCH, M.D. London: Research Books Ltd., 1946. Pp. xi and 312. Price 21s.

ALTHOUGH this book is essentially for the specialist it contains much information of practical value for the general medical reader, avoiding to a much greater extent than usual the obscurities which the overuse of a specialized vocabulary so often involves. The writer is a disciple of Freud but holds her own opinions throughout—for example, she draws constant attention to the differences between male and female development even in pre-pubertal years, a point so often overlooked in this type of

literature. The different stages of feminine development are dealt with in an expert manner and clearly from much personal clinical experience. The chapters on the pre-pubertal and menopausal periods particularly, contain much that is of value. Later chapters on the more special and the abnormal developments of feminine psychology are of much interest, although it might perhaps be said that the structural and constitutional aspects of the author's cases are not taken sufficiently into account. This book is certainly worth reading.

The British Encyclopædia of Medical Practice: Medical Progress and Cumulative Supplement, 1946. Edited by the RT. HON. LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P. London: Butterworth & Co. (Publishers) Ltd., 1946. Pp. v, 458 and 40 and 267. Price 37s. 6d.

ONE of the most welcome inclusions in Medical Progress 1946, is a chapter on penicillin by Sir Howard Florey, in which he gives a full survey of the knowledge and uses of penicillin up to date, with methods of administration, dosage and the value of penicillin in the treatment of different diseases. The chapter on mental diseases, by the late R. D. Gillespie, will be read with interest and deep regret as the last that will come from his pen. In the introduction the Editor in Chief pays a graceful tribute to the late Sir Humphry Rolleston and his irreplaceable work in the field of medical literature.

NEW EDITIONS

IN the preparation of the fifth edition of *The Nervous Child*, by H. C. Cameron, M.D., F.R.C.P. (Oxford University Press, 10s. 6d.) rewriting has not been undertaken, but the author has added several new sections dealing respectively with umbilical colic, night terrors, vomiting in infancy and excessive depth of sleep in enuresis. The prevention of nervous phenomena in children is a subject of general interest to practitioners, who will find in this little book much practical advice which does not impinge on the nowadays somewhat overstressed field of psychiatry.

Medical Emergencies, by CHARLES NEWMAN, M.D., F.R.C.P., in its third edition (J. & A. Churchill Ltd., 10s. 6d.) has been subjected to a number of alterations, and sections on the sulphonamides and penicillin have been added. The author's method of a brief outline of the symptoms followed by instructions for treatment makes this book a valuable addition to the everyday library of the practitioner.

REVIEWS OF BOOKS

The Peripheral Circulation in Health and Disease. By ROBERT L. RICHARDS, M.D. Foreword by PROFESSOR J. R. LEARMONTH, C.B.E., CH.M., F.R.C.S.ED. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. xii and 153. Figures 104. Price 21s.

THIS handsomely produced monograph is a useful contribution to a highly specialized branch of medicine. Based upon an investigation carried out in Edinburgh, under the direction of Professor Learmonth, it provides an excellent example of how clinical investigation should be carried out. Introductory chapters are devoted to the anatomy and physiology of the peripheral vasomotor system and methods of study of the system. These are followed by chapters on occlusive vascular disease, the Raynaud phenomenon, peripheral nerve injuries and the immersion foot syndrome. An extensive bibliography adds considerably to the value of the work. In face of this carefully accumulated wealth of information it is a humbling thought that over eighty years have passed since Raynaud first described the condition to which his name is attached; for to-day, in spite of all the careful work on the subject that has been done during two world wars, "clinical science" has added many stones to the edifice, but it has failed to provide the coping stone that will complete the edifice. Indeed, the more data that issue from the laboratory (clinical or physiological), the more complex does the problem appear. As an attempt not merely to add to the sum total of factual data, but to merge the known facts into a recognized pattern, this monograph will be welcomed by all who have an interest in this intriguing problem of the peripheral circulation and its disorders.

Ancient Anodynes. By E. S. ELLIS, M.R.C.S., F.R.A.I. With Foreword by T. K. PENNIMAN, M.A. London: William Heinemann (Medical Books) Ltd., 1946. Pp. 187. Price 21s.

THIS book, appropriately appearing in the centenary year of ether, will be of interest to both medical men and anthropologists. Using the term "anæsthesia" in a wide sense, the author has dealt with the many methods which have been used throughout the ages to assuage pain. This covers a vast field from primitive man down to the introduction of chloroform as an anæsthetic. As is inevitable in dealing with ancient usages, considerable space is devoted to the use of inebriants, until quite recent times one of the most widely used methods of relieving pain. An amazing amount of information is packed into these pages, and this, combined with the rather stilted style in which the book is written, does not make for easy reading. As it is primarily a reference book, however, this criticism does not detract from its essential value. On the other hand, it is a pity that a fuller index has not been provided. The scope of the book is well summed up in the foreword by the Curator of the Pitt Rivers Museum in the University of Oxford: "Here can be found a vast number of ways by which humanity has attempted to assuage its ills . . . Dr. Ellis, with his medical knowledge, has been able to assess their value, medically and psychologically".

How a Baby Grows. By ARNOLD GESELL, M.D. London: Hamish Hamilton, Medical Books, 1946. Pp. vii and 78. Price 10s. 6d.

THIS is a profusely illustrated book, with a series of short commentaries by the famous director of the Yale Clinic of Child Development. The photographs are selected from the cinematographic records and "still" pictures prepared over a seven-years period for the *Atlas of Infant Behaviour.* The present volume is obviously more intended for parents than for the scientific student of infant and child development, but it should prove a useful reference work for all those concerned with children. The photographs are beautifully reproduced and skilfully arranged, covering various aspects of the baby and child during the first five years of life.

Analecta Psychiatrica. By J. R. WHITWELL, M.B. London: H. K. Lewis & Co., Ltd., 1946. Pp. 160. Price 16s.

THE author of this book, a former superintendent of a mental hospital, is the honorary librarian of the Royal Medico-Psychological Association. "This collection of psychiatric miscellanies", as Dr. Whitwell describes it in his preface, makes fascinating reading. Taking the whole range of literature from Plato to Wordsworth as his field, he has amassed a wealth of sayings of the great figures of literature concerning mental disorders. These quotations are divided into sections dealing with forms of mental disorder, suicide, causes of mental disorder, treatment, and pathology. The concluding section deals with "some interesting cases" of insanity, including Samuel John-

DIABETES MELLITUS 1921-46
By ELLIOTT P. JOSLIN, M.D.
Boston, U.S.A.

To the British Commonwealth of Nations medicine is indebted for three notable advances in diabetes during the last twenty-five years—the discovery of insulin by Banting and Best in Toronto, the culminating demonstration of the production of diabetes by injections of an extract of the anterior pituitary gland by Young in London, and the wholly unexpected discovery of the destruction of the islands of Langerhans with alloxan by Dunn, Sheehan and McLetchie in Glasgow. From America have come mass demonstrations bearing on the incidence and improvement in the treatment of the disease. Less spectacular but of great fundamental importance has been the expansion of knowledge regarding the utilization of carbohydrate by the diabetic, including the relation of insulin and the place of hexokinase in its metabolism, and the revision of concepts regarding the etiology of acidosis.

In my view, the three impressive results of the discovery of insulin are: first, the practical abolition of coma; second, the lengthening lives and increased efficiency of diabetics; and, third, the possibility and safety of pregnancy in the diabetic woman.

THE PRACTICAL ABOLITION OF DIABETIC COMA

Before *1914*, both *von Noorden and I each saw approximately two-thirds* of our patients dying of diabetic coma, and even with the introduction of the theory of undernutrition by F. M. Allen this mortality was only lowered to 40 per cent. by 1922. Yet at that time those most concerned and most actively interested in the care of diabetics were able to record that only rarely would diabetic coma develop in a hospital with the patient under good medical care, and the slogan arose "make diabetes as safe in the home as in the hospital." An occasional case of early diabetic acidosis was rescued and, in fact, just before entering the Army in January 1918, I reported 15 such cases with a carbon dioxide combining power of the blood of 20 volumes per cent. or less. But in general the rescue of an advanced case was considered hopeless, either in or outside the hospital. In contrast, I record in table 1 the decrease in the percentage of deaths from coma among the total

NOTES AND PREPARATIONS

ROYAL MEDICAL BENEVOLENT FUND: "CHRISTMAS GIFTS"

SIR ARNOLD LAWSON, President of the Royal Medical Benevolent Fund, in his annual Christmas appeal letter, writes:—

"The reasons for this Appeal are now well known to all your readers and there is no reason to stress them again. I would rather emphasize the point that they are as cogent as ever. It is true that the Old Age Pension which is now in force, whilst making the financial position of old people more bearable, still means that the actual increase in annual income is only £41 12s. p.a., which, bearing in mind the tremendous increase in the cost of living, still makes the position of the poor housewife very difficult indeed. Further, many of our beneficiaries are under 70 years of age and so are not able to draw the pension. Lastly, there is that very real sense of being 'not forgotten' at the festive time of Christmas and the knowledge that our Christmas Gift will ensure the purchase of a few extra luxuries which just make all the difference."

In answer to the appeal for a sum of £2,000 last year, so as to allow a gift of £4 to each beneficiary, the total sum received reached £2,127, and Sir Arnold continues:—

" . . . I know every generous donor will feel amply repaid by the gratitude and pleasure these gifts have evoked. May I venture to plead for a similar sum this year? I feel sure that, although I well recognize that times are very difficult for everybody just now, the still greater difficulties and anxieties of our very poor brethren will not pass unheeded."

Contributions, marked "Christmas Gifts", should be forwarded to the Secretary, Royal Medical Benevolent Fund, 1 Balliol House, Manor Fields, Putney, London, S.W.15.

STREPTOMYCIN

AT a conference held at the London headquarters of Boots Pure Drug Co. Ltd. on October 1, Sir Jack Drummond, D.Sc., F.R.S., Director in charge of the Company's scientific research, discussed the properties and the prospects of streptomycin. This antibiotic substance, which has been isolated from *Actinomyces Griseus*, is closely allied to penicillin but possesses the advantages of being more stable and of being active against gram-negative organisms. In America, where most of the work with streptomycin has so far been carried out, encouraging results have been obtained in the treatment of tuberculosis (*The Practitioner*, 1946, **156**, 218), although it is not yet known whether the improvement with streptomycin therapy represents a temporary arrest of the condition or a cure. Good results have also been obtained in meningitis due to *B. influenzæ*, and in tularæmia a 100 per cent. cure rate has been reported. The production of streptomycin is long and costly; according to American estimates the treatment of a single tuberculous patient costs approximately £3,000 with production by the surface culture method. Messrs. Boots have set up a pilot plant for production by surface culture. Increased production is already under way and in a few weeks a sufficient quantity of streptomycin will be made available to the Ministry of Health for controlled tests on a limited number of patients, the results of which will be awaited with interest.

LONDON MEDICAL EXHIBITION

THE twenty-ninth annual London Medical Exhibition will open on Monday, November 18, at the New Hall of the Royal Horticultural Society, Greycoat Street, Westminster, S.W.1, and will remain open daily from 11 a.m. to 6.30 p.m. until Friday, November 22. Admission is confined to members of the medical and dental professions, and invitations are issued by the organizers, the British and Colonial Druggists Ltd., 194-200 Bishopsgate, E.C.2. Doctors who do not receive invitations should apply to the organizers, or present their professional cards at the entrance to the Hall.

DIPHTHERIA IMMUNIZATION

AT the opening of the 105th session of the College of the Pharmaceutical Society on October 2, Sir Percival Hartley, F.R.S., Director of Biological Standards at the National Institute of Medical Research, said that the Ministry of Health's campaign against diphtheria had met with remarkable success. The incidence and death rates had fallen. The present high standard must be maintained, however, by immunizing the greatest possible number of children.

NEW MEDICAL PUBLICATIONS

THE first number of *Anæsthesia*, the journal of the Association of Anæsthetists of Great Britain and Ireland, appeared in October. The publication of the first issue of this journal in the year of the centenary of anæsthesia in Great Britain is a happy augury of its success. The Editor is Dr. C. Langton Hewer, and the Sub-Editor, Dr. R. Blair Gould. The journal is published quarterly, price 10s., by George Pulman and Sons, Ltd., for the Association of Anæsthetists of Great Britain and Ireland, 24 Thayer Street, London, W.1.

THE new quarterly *Journal of the History of Medicine and Allied Sciences* will in future be issued in this country and the British Empire by William Heinemann (Medical Books) Ltd., 99 Great Russell Street, London, W.C.1. Volume 1, no. 3, will be available within the next few weeks. The English subscription rate is 50s. per annum for four issues: 12s. 6d. per single issue.

Our method of treatment has often been described.

(1) Being sure of the diagnosis: give crystalline or unmodified insulin early and enough: 25, 50 or 100 units immediately and repeat every thirty or sixty minutes as necessary.

(2) Correct dehydration by adequate amounts of normal saline parenterally.

(3) Empty the stomach gently by stomach tube (a) to prevent its dilatation, (b) to remove collected residual food and often blood and (c) to guard against involuntary vomiting into the lung or (d) cardiac collapse due to gastric distension.

(4) Concentrated nursing for half a dozen hours to save diluted nursing for a whole day.

(5) Hunt for, diagnose and treat vigorously the complication which may have brought on the coma. Relieve a distended rectum.

(7) Do sufficient blood sugar tests, usually by capillary blood to save the veins, so that as soon as hyperglycæmia and acidosis are well on the way to being controlled, carbohydrate and broths and simple food can be given by mouth or vein. We do not use alkalis. We do not give glucose until the hyperglycæmia is under control, and only then if food given orally is not retained.

The knowledge that diabetic coma is needless and that non-recognition of the existence of diabetes, ignorance or carelessness account for it, are prime factors in the combat with deaths from it. But, to attack it successfully, the patient needs the benefit of immediate hospital care with laboratory facilities available for the doctor day and night, Sundays and holidays.

THE LENGTHENING LIVES OF DIABETICS

Diabetics are living longer than they did a quarter of a century ago—at least three times as long. The figures in table 3 are based on fatal cases: this must not be overlooked. We still have survivors of the Naunyn era, and if we include their long durations, our total average duration for that era instead of being 4.9 years, in 1940 was 9.4 years, for the Allen era 11.9 years instead of 6.1 years, and for the remaining eras, doubtless the accretions due to the inclusion of living cases will be far more. This is especially true if the early age-groups are studied. Thus the duration of life of the 15 fatal cases in the first decade in the most recent era should be compared with the 249 cases with onset under fifteen years of age who have lived for over twenty years. So recently as the period 1937-43, our patients living twenty or more years constituted only 15 per cent. of the total deaths, but between 1944 and May 15, 1946, they have reached 22 per cent., i.e., more than one-fifth of all our cases live over twenty years, which is nearly the expectancy of everyone completing his fiftieth year of age, the age above which approximately half the cases of diabetes begin.

causes of death of 8,384 of my patients. The most recent compilations show graphically what has transpired in my practice. At the same time it should be made clear that these statistics are based upon diabetics seen at times only once, although usually cared for during a considerable period of time, but later dying anywhere in the world and thus not under the immediate care of our group. The facts here portrayed therefore demonstrate a universal advance in the treatment of diabetics, each successive era showing a fall in mortality and reaching 3.1 per cent. in the most recent series.

TABLE 1

THE REDUCTION IN MORTALITY FROM DIABETIC COMA AMONG 8,384 FATAL CASES OF DIABETES

Era	Percentage of deaths from coma to all deaths
Naunyn, 1898—1914	63.8
Allen, 1914—1922	41.5
Banting, 1922—1936	8.4
Hagedorn, 1937—1943	3.4
Charles H. Best, 1944—May 15, 1946	3.1

The specific treatment of coma, as well as the reports of deaths due to coma, have been gratifying. I deprecate comparisons in results of treatment between different clinics. Such comparisons become too involved in details and miss the point. What is of more importance and what all of us really wish to know is whether our own treatment in our own group of cases is better now than a quarter of a century, a decade or even five years ago for patients measured by the same criteria of depth of acidosis. Therefore in table 2 are summarized our results in patients treated for coma at the Deaconess Hospital. They show that whereas before 1940, 12.1 per cent. of our coma cases died, between 1940 and 1946 we lost only 1.2 per cent.

TABLE 2

DECLINE IN MORTALITY IN DIABETIC COMA CASES TREATED AT THE NEW ENGLAND DEACONESS HOSPITAL

	Jan. 1923—Aug. 1940	Aug. 1940—Dec. 31, 1945
No. of cases	478	173
No. of deaths	58	3
Percentage of deaths	12.1	1.2

And why ? Simply because to-day, although on the average the same amount of insulin is given, we give it in the first *three* hours rather than distribute it over the first twelve hours. Thus, in the early insulin period 83 units were administered in the first three hours, in contrast to the 212 units in our more recent series. Accessories of treatment have been essentially unaltered. These few figures exemplify what can be done to improve treatment and the necessity of making it possible for all doctors to carry it out and for patients to receive it.

Our method of treatment has often been described.

(1) Being sure of the diagnosis: give crystalline or unmodified insulin early and enough: 25, 50 or 100 units immediately and repeat every thirty or sixty minutes as necessary.

(2) Correct dehydration by adequate amounts of normal saline parenterally.

(3) Empty the stomach gently by stomach tube (a) to prevent its dilatation, (b) to remove collected residual food and often blood and (c) to guard against involuntary vomiting into the lung or (d) cardiac collapse due to gastric distension.

(4) Concentrated nursing for half a dozen hours to save diluted nursing for a whole day.

(5) Hunt for, diagnose and treat vigorously the complication which may have brought on the coma. Relieve a distended rectum.

(7) Do sufficient blood sugar tests, usually by capillary blood to save the veins, so that as soon as hyperglycæmia and acidosis are well on the way to being controlled, carbohydrate and broths and simple food can be given by mouth or vein. We do not use alkalis. We do not give glucose until the hyperglycæmia is under control, and only then if food given orally is not retained.

The knowledge that diabetic coma is needless and that non-recognition of the existence of diabetes, ignorance or carelessness account for it, are prime factors in the combat with deaths from it. But, to attack it successfully, the patient needs the benefit of immediate hospital care with laboratory facilities available for the doctor day and night, Sundays and holidays.

THE LENGTHENING LIVES OF DIABETICS

Diabetics are living longer than they did a quarter of a century ago—at least three times as long. The figures in table 3 are based on fatal cases: this must not be overlooked. We still have survivors of the Naunyn era, and if we include their long durations, our total average duration for that era instead of being 4.9 years, in 1940 was 9.4 years, for the Allen era 11.9 years instead of 6.1 years, and for the remaining eras, doubtless the accretions due to the inclusion of living cases will be far more. This is especially true if the early age-groups are studied. Thus the duration of life of the 15 fatal cases in the first decade in the most recent era should be compared with the 249 cases with onset under fifteen years of age who have lived for over twenty years. So recently as the period 1937-43, our patients living twenty or more years constituted only 15 per cent. of the total deaths, but between 1944 and May 15, 1946, they have reached 22 per cent., i.e., more than one-fifth of all our cases live over twenty years, which is nearly the expectancy of everyone completing his fiftieth year of age, the age above which approximately half the cases of diabetes begin.

causes of death of 8,384 of my patients. The most recent compilations show graphically what has transpired in my practice. At the same time it should be made clear that these statistics are based upon diabetics seen at times only once, although usually cared for during a considerable period of time, but later dying anywhere in the world and thus not under the immediate care of our group. The facts here portrayed therefore demonstrate a universal advance in the treatment of diabetics, each successive era showing a fall in mortality and reaching 3.1 per cent. in the most recent series.

TABLE 1

THE REDUCTION IN MORTALITY FROM DIABETIC COMA AMONG 8,384 FATAL CASES OF DIABETES

Era	Percentage of deaths from coma to all deaths
Naunyn, 1898—1914	63.8
Allen, 1914—1922	41.5
Banting, 1922—1936	8.4
Hagedorn, 1937—1943	3.4
Charles H. Best, 1944—May 15, 1946	3.1

The specific treatment of coma, as well as the reports of deaths due to coma, have been gratifying. I deprecate comparisons in results of treatment between different clinics. Such comparisons become too involved in details and miss the point. What is of more importance and what all of us really wish to know is whether our own treatment in our own group of cases is better now than a quarter of a century, a decade or even five years ago for patients measured by the same criteria of depth of acidosis. Therefore in table 2 are summarized our results in patients treated for coma at the Deaconess Hospital. They show that whereas before 1940, 12.1 per cent. of our coma cases died, between 1940 and 1946 we lost only 1.2 per cent.

TABLE 2

DECLINE IN MORTALITY IN DIABETIC COMA CASES TREATED AT THE NEW ENGLAND DEACONESS HOSPITAL

	Jan. 1923—Aug. 1940	Aug. 1940—Dec. 31, 1945
No. of cases	478	173
No. of deaths	58	3
Percentage of deaths	12.1	1.2

And why? Simply because to-day, although on the average the same amount of insulin is given, we give it in the first *three* hours rather than distribute it over the first twelve hours. Thus, in the early insulin period 83 units were administered in the first three hours, in contrast to the 212 units in our more recent series. Accessories of treatment have been essentially unaltered. These few figures exemplify what can be done to improve treatment and the necessity of making it possible for all doctors to carry it out and for patients to receive it.

Our method of treatment has often been described.

(1) Being sure of the diagnosis: give crystalline or unmodified insulin early and enough: 25, 50 or 100 units immediately and repeat every thirty or sixty minutes as necessary.

(2) Correct dehydration by adequate amounts of normal saline parenterally.

(3) Empty the stomach gently by stomach tube (a) to prevent its dilatation, (b) to remove collected residual food and often blood and (c) to guard against involuntary vomiting into the lung or (d) cardiac collapse due to gastric distension.

(4) Concentrated nursing for half a dozen hours to save diluted nursing for a whole day.

(5) Hunt for, diagnose and treat vigorously the complication which may have brought on the coma. Relieve a distended rectum.

(7) Do sufficient blood sugar tests, usually by capillary blood to save the veins, so that as soon as hyperglycæmia and acidosis are well on the way to being controlled, carbohydrate and broths and simple food can be given by mouth or vein. We do not use alkalis. We do not give glucose until the hyperglycæmia is under control, and only then if food given orally is not retained.

The knowledge that diabetic coma is needless and that non-recognition of the existence of diabetes, ignorance or carelessness account for it, are prime factors in the combat with deaths from it. But, to attack it successfully, the patient needs the benefit of immediate hospital care with laboratory facilities available for the doctor day and night, Sundays and holidays.

THE LENGTHENING LIVES OF DIABETICS

Diabetics are living longer than they did a quarter of a century ago—at least three times as long. The figures in table 3 are based on fatal cases: this must not be overlooked. We still have survivors of the Naunyn era, and if we include their long durations, our total average duration for that era instead of being 4.9 years, in 1940 was 9.4 years, for the Allen era 11.9 years instead of 6.1 years, and for the remaining eras, doubtless the accretions due to the inclusion of living cases will be far more. This is especially true if the early age-groups are studied. Thus the duration of life of the 15 fatal cases in the first decade in the most recent era should be compared with the 249 cases with onset under fifteen years of age who have lived for over twenty years. So recently as the period 1937-43, our patients living twenty or more years constituted only 15 per cent. of the total deaths, but between 1944 and May 15, 1946, they have reached 22 per cent., i.e., more than one-fifth of all our cases live over twenty years, which is nearly the expectancy of everyone completing his fiftieth year of age, the age above which approximately half the cases of diabetes begin.

causes of death of 8,384 of my patients. The most recent compilations show graphically what has transpired in my practice. At the same time it should be made clear that these statistics are based upon diabetics seen at times only once, although usually cared for during a considerable period of time, but later dying anywhere in the world and thus not under the immediate care of our group. The facts here portrayed therefore demonstrate a universal advance in the treatment of diabetics, each successive era showing a fall in mortality and reaching 3.1 per cent. in the most recent series.

TABLE 1

THE REDUCTION IN MORTALITY FROM DIABETIC COMA AMONG 8,384 FATAL CASES OF DIABETES

Era	Percentage of deaths from coma to all deaths
Naunyn, 1898—1914	63.8
Allen, 1914—1922	41.5
Banting, 1922—1936	8.4
Hagedorn, 1937—1943	3.4
Charles H. Best, 1944—May 15, 1946	3.1

The specific treatment of coma, as well as the reports of deaths due to coma, have been gratifying. I deprecate comparisons in results of treatment between different clinics. Such comparisons become too involved in details and miss the point. What is of more importance and what all of us really wish to know is whether our own treatment in our own group of cases is better now than a quarter of a century, a decade or even five years ago for patients measured by the same criteria of depth of acidosis. Therefore in table 2 are summarized our results in patients treated for coma at the Deaconess Hospital. They show that whereas before 1940, 12.1 per cent. of our coma cases died, between 1940 and 1946 we lost only 1.2 per cent.

TABLE 2

DECLINE IN MORTALITY IN DIABETIC COMA CASES TREATED AT THE NEW ENGLAND DEACONESS HOSPITAL

	Jan. 1923—Aug. 1940	Aug. 1940—Dec. 31, 1945
No. of cases	478	173
No. of deaths	58	3
Percentage of deaths	12.1	1.2

And why? Simply because to-day, although on the average the same amount of insulin is given, we give it in the first *three* hours rather than distribute it over the first twelve hours. Thus, in the early insulin period 83 units were administered in the first three hours, in contrast to the 212 units in our more recent series. Accessories of treatment have been essentially unaltered. These few figures exemplify what can be done to improve treatment and the necessity of making it possible for all doctors to carry it out and for patients to receive it.

Our method of treatment has often been described.

(1) Being sure of the diagnosis: give crystalline or unmodified insulin early and enough: 25, 50 or 100 units immediately and repeat every thirty or sixty minutes as necessary.

(2) Correct dehydration by adequate amounts of normal saline parenterally.

(3) Empty the stomach gently by stomach tube (a) to prevent its dilatation, (b) to remove collected residual food and often blood and (c) to guard against involuntary vomiting into the lung or (d) cardiac collapse due to gastric distension.

(4) Concentrated nursing for half a dozen hours to save diluted nursing for a whole day.

(5) Hunt for, diagnose and treat vigorously the complication which may have brought on the coma. Relieve a distended rectum.

(7) Do sufficient blood sugar tests, usually by capillary blood to save the veins, so that as soon as hyperglycæmia and acidosis are well on the way to being controlled, carbohydrate and broths and simple food can be given by mouth or vein. We do not use alkalis. We do not give glucose until the hyperglycæmia is under control, and only then if food given orally is not retained.

The knowledge that diabetic coma is needless and that non-recognition of the existence of diabetes, ignorance or carelessness account for it, are prime factors in the combat with deaths from it. But, to attack it successfully, the patient needs the benefit of immediate hospital care with laboratory facilities available for the doctor day and night, Sundays and holidays.

THE LENGTHENING LIVES OF DIABETICS

Diabetics are living longer than they did a quarter of a century ago—at least three times as long. The figures in table 3 are based on fatal cases: this must not be overlooked. We still have survivors of the Naunyn era, and if we include their long durations, our total average duration for that era instead of being 4.9 years, in 1940 was 9.4 years, for the Allen era 11.9 years instead of 6.1 years, and for the remaining eras, doubtless the accretions due to the inclusion of living cases will be far more. This is especially true if the early age-groups are studied. Thus the duration of life of the 15 fatal cases in the first decade in the most recent era should be compared with the 249 cases with onset under fifteen years of age who have lived for over twenty years. So recently as the period 1937-43, our patients living twenty or more years constituted only 15 per cent. of the total deaths, but between 1944 and May 15, 1946, they have reached 22 per cent., i.e., more than one-fifth of all our cases live over twenty years, which is nearly the expectancy of everyone completing his fiftieth year of age, the age above which approximately half the cases of diabetes begin.

TABLE 3

AVERAGE DURATION OF LIFE SUBSEQUENT TO ONSET OF DIABETES AMONG DECEASED
EX-PATIENTS (Experience of ELLIOTT P. JOSLIN, M.D., 1914—1946)

Age groups of onset	Allen era June 1, 1914 to Aug. 6, 1922		Banting era Aug. 7, 1922 to Dec. 31, 1936		Hagedorn era Jan. 1, 1937 to Dec. 31, 1943		Charles H. Best era Jan. 1, 1944 to date†	
	No. of cases	Duration yrs	No. of cases	Duration yrs	No. of cases	Duration yrs	No. of cases	Duration yrs
All ages	836	6.1	3989	9.6*	2583	12.9	651	14.1
0—10	61	2.9	45	5.2	35	10.2	15	16.7
10—19	84	2.7	112	5.5	71	11.1	31	13.2
20—39	215	4.9	464	12.2	299	17.4	70	17.9
40—59	351	8.0	2175	11.0	1373	14.4	328	16.2
60 and over	117	6.4	1173	6.6	804	9.0	200	9.3
Unknown	8	—	20	—	1	—	7	—

† Deaths reported up to May 15, 1946.
* Based on cases with known duration.
   Prepared by the Statistical Bureau of the Metropolitan Life Insurance Company.

If these figures simply meant prolongation of existence there would be little satisfaction in striving for their attainment; but they mean far more. That there is a wonderful increase in the efficiency of diabetics is well known. Much is heard about the growing percentage of old people in the world: if they generally could grow in efficiency, as have our diabetics, what a miracle it would be! What an example is afforded of efficiency produced by medical science. It gives hope for attacking the problem of growing old. It is up to us doctors to prove that our diabetics, even over sixty-five years of age, can amount to something.

And this brings me to a sobering thought. Are we doing all we can to preserve the health of our childhood diabetics so that after twenty years of the disease they will be happy and healthy? I know I have not done enough. Of 249 cases in this group, after completing twenty years of the disease, only 30 per cent. are free from complications in the eyes, kidneys and heart. Again here, I care comparatively little about results in other clinics: what I want and my colleagues want is to improve the treatment of our own children. It is only fair to ourselves to point out that these 249 cases should represent the worst possible series of cases we shall ever report, because so many of them illustrate the results of treatment begun before the advent of insulin and all began it when diet was unnecessarily low in carbohydrate and calories. Although for the child diabetic the outlook for the second twenty years of diabetes is threatening, it should never be as bad as these early statistics imply.

There is not the slightest particle of doubt in my own mind that the diabetic child who has the greatest number of well-treated and honestly

lived diabetic days to his credit is the one who will make the best showing at the end of his first twenty years of the disease. This is the principle underlying improved treatment of the youthful diabetic which I am positive should be preached. If we can only defer or make headway against the arteriosclerotic complications of diabetes in the young, there will be hope for their partial arrest in the old. Moreover, what is learned about arteriosclerosis generally in diabetics may be applied to non-diabetics. There is far more in this problem of conquering diabetes than is generally realized.

THE POSSIBILITY AND SAFETY OF PREGNANCY IN THE DIABETIC

When *Case no.* 604 died of diabetic coma during delivery, the baby was lost and the father shot himself. I thereupon published forthwith every single case of a pregnant diabetic I had seen up to that time. Bouchardat never saw a pregnant diabetic woman and Naunyn records but one in 1907. On this very day, when I am writing this article, July 31, 1946, Dr. Priscilla White of our group tells me that she now has under her immediate supervision 46 pregnant diabetic women; that of 273 delivered since January 1, 1936, there has been but one death, and that instead of saving 50 babies out of a hundred before that date, she now has actually saved 90 per cent., and in the group of those mothers whom she has had a fair opportunity to treat, the live babies are 90 per cent. For details of management I must refer to her writings. I frankly admit that her remarkable results, which I have seen with my own eyes, must be tempered in their evaluation by the knowledge that she has devoted herself largely to diabetes for more than twenty years and has certainly been involved in the treatment of 25,000 glycosuric cases, that her patients have had the advantage of the cooperation of a single obstetrician, Dr. Raymond S. Titus, of having all the deliveries take place at the Faulkner Hospital, which has a large obstetrical department, and that she has had placed at her disposal the same head nurse and, finally, has benefited from the friendly cooperation of the same pædiatrician, Dr. Warren R. Sisson.

Let me give one illustration of Dr. Priscilla White's care of her pregnant brood. I am writing this paper at my summer home on a hill in Oxford, Massachusetts, fifty miles from Boston. To the south is the old fort built by the Huguenots in 1687, later to be abandoned because of an Indian massacre, the town being resettled by the English in 1713. To the west is Charlton, the birthplace of Morton, who first gave ether to a patient in 1846, the hundredth anniversary of which is celebrated by the Massachusetts General Hospital this year. To the south-west is Webster, where Slater brought to America in his head the first cotton machinery from England. To the north-west is the birthplace of Clara Barton, who originated the Red Cross in the United States and on whose father's land at this moment is our summer camp for 120 diabetic children. And over to the west is another farm on which lives one of Priscilla White's pregnant diabetics. This patient felt a little out of sorts on July 22, and having been previously at the camp, the senior camp nurse, Miss Patricia MacHugh, noted she was dehydrated and that the urine contained acetone and diacetic acid. Two hours later she reached the New England

TABLE 3

AVERAGE DURATION OF LIFE SUBSEQUENT TO ONSET OF DIABETES AMONG DECEASED EX-PATIENTS (Experience of ELLIOTT P. JOSLIN, M.D., 1914—1946)

Age groups of onset	Allen era June 1, 1914 to Aug. 6, 1922		Banting era Aug. 7, 1922 to Dec. 31, 1936		Hagedorn era Jan. 1, 1937 to Dec. 31, 1943		Charles H. Best era Jan. 1, 1944 to date†	
	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs
All ages	836	6.1	3989	9.6*	2583	12.9	651	14.1
0—10	61	2.9	45	5.2	35	10.2	15	16.7
10—19	84	2.7	112	5.5	71	11.1	31	13.2
20—39	215	4.9	464	12.2	299	17.4	70	17.9
40—59	351	8.0	2175	11.0	1373	14.4	328	16.2
60 and over	117	6.4	1173	6.6	804	9.0	200	9.3
Unknown	8	—	20		1	—	7	—

† Deaths reported up to May 15, 1946.
* Based on cases with known duration.
Prepared by the Statistical Bureau of the Metropolitan Life Insurance Company.

If these figures simply meant prolongation of existence there would be little satisfaction in striving for their attainment; but they mean far more. That there is a wonderful increase in the efficiency of diabetics is well known. Much is heard about the growing percentage of old people in the world: if they generally could grow in efficiency, as have our diabetics, what a miracle it would be! What an example is afforded of efficiency produced by medical science. It gives hope for attacking the problem of growing old. It is up to us doctors to prove that our diabetics, even over sixty-five years of age, can amount to something.

And this brings me to a sobering thought. Are we doing all we can to preserve the health of our childhood diabetics so that after twenty years of the disease they will be happy and healthy? I know I have not done enough. Of 249 cases in this group, after completing twenty years of the disease, only 30 per cent. are free from complications in the eyes, kidneys and heart. Again here, I care comparatively little about results in other clinics: what I want and my colleagues want is to improve the treatment of our own children. It is only fair to ourselves to point out that these 249 cases should represent the worst possible series of cases we shall ever report, because so many of them illustrate the results of treatment begun before the advent of insulin and all began it when diet was unnecessarily low in carbohydrate and calories. Although for the child diabetic the outlook for the second twenty years of diabetes is threatening, it should never be as bad as these early statistics imply.

There is not the slightest particle of doubt in my own mind that the diabetic child who has the greatest number of well-treated and honestly

lived diabetic days to his credit is the one who will make the best showing at the end of his first twenty years of the disease. This is the principle underlying improved treatment of the youthful diabetic which I am positive should be preached. If we can only defer or make headway against the arteriosclerotic complications of diabetes in the young, there will be hope for their partial arrest in the old. Moreover, what is learned about arteriosclerosis generally in diabetics may be applied to non-diabetics. There is far more in this problem of conquering diabetes than is generally realized.

THE POSSIBILITY AND SAFETY OF PREGNANCY IN THE DIABETIC

When *Case no.* 604 died of diabetic coma during delivery, the baby was lost and the father shot himself. I thereupon published forthwith every single case of a pregnant diabetic I had seen up to that time. Bouchardat never saw a pregnant diabetic woman and Naunyn records but one in 1907. On this very day, when I am writing this article, July 31, 1946, Dr. Priscilla White of our group tells me that she now has under her immediate supervision 46 pregnant diabetic women; that of 273 delivered since January 1, 1936, there has been but one death, and that instead of saving 50 babies out of a hundred before that date, she now has actually saved 90 per cent., and in the group of those mothers whom she has had a fair opportunity to treat, the live babies are 90 per cent. For details of management I must refer to her writings. I frankly admit that her remarkable results, which I have seen with my own eyes, must be tempered in their evaluation by the knowledge that she has devoted herself largely to diabetes for more than twenty years and has certainly been involved in the treatment of 25,000 glycosuric cases, that her patients have had the advantage of the cooperation of a single obstetrician, Dr. Raymond S. Titus, of having all the deliveries take place at the Faulkner Hospital, which has a large obstetrical department, and that she has had placed at her disposal the same head nurse and, finally, has benefited from the friendly cooperation of the same pædiatrician, Dr. Warren R. Sisson.

Let me give one illustration of Dr. Priscilla White's care of her pregnant brood. I am writing this paper at my summer home on a hill in Oxford, Massachusetts, fifty miles from Boston. To the south is the old fort built by the Huguenots in 1687, later to be abandoned because of an Indian massacre, the town being resettled by the English in 1713. To the west is Charlton, the birthplace of Morton, who first gave ether to a patient in 1846, the hundredth anniversary of which is celebrated by the Massachusetts General Hospital this year. To the south-west is Webster, where Slater brought to America in his head the first cotton machinery from England. To the north-west is the birthplace of Clara Barton, who originated the Red Cross in the United States and on whose father's land at this moment is our summer camp for 120 diabetic children. And over to the west is another farm on which lives one of Priscilla White's pregnant diabetics. This patient felt a little out of sorts on July 22, and having been previously at the camp, the senior camp nurse, Miss Patricia MacHugh, noted she was dehydrated and that the urine contained acetone and diacetic acid. Two hours later she reached the New England

TABLE 3

AVERAGE DURATION OF LIFE SUBSEQUENT TO ONSET OF DIABETES AMONG DECEASED
EX-PATIENTS (Experience of ELLIOTT P. JOSLIN, M.D., 1914—1946)

Age groups of onset	Allen era June 1, 1914 to Aug. 6, 1922		Banting era Aug. 7, 1922 to Dec. 31, 1936		Hagedorn era Jan. 1, 1937 to Dec. 31, 1943		Charles H. Best era Jan. 1, 1944 to date†	
	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs	No. of cases	Dura-tion yrs
All ages	836	6.1	3989	9.6*	2583	12.9	651	14.1
0—10	61	2.9	45	5.2	35	10.2	15	16.7
10—19	84	2.7	112	5.5	71	11.1	31	13.2
20—39	215	4.9	464	12.2	299	17.4	70	17.9
40—59	351	8.0	2175	11.0	1373	14.4	328	16.2
60 and over	117	6.4	1173	6.6	804	9.0	200	9.3
Unknown	8	—	20	—	1	—	7	—

† Deaths reported up to May 15, 1946.
* Based on cases with known duration.
Prepared by the Statistical Bureau of the Metropolitan Life Insurance Company.

If these figures simply meant prolongation of existence there would be little satisfaction in striving for their attainment; but they mean far more. That there is a wonderful increase in the efficiency of diabetics is well known. Much is heard about the growing percentage of old people in the world: if they generally could grow in efficiency, as have our diabetics, what a miracle it would be! What an example is afforded of efficiency produced by medical science. It gives hope for attacking the problem of growing old. It is up to us doctors to prove that our diabetics, even over sixty-five years of age, can amount to something.

And this brings me to a sobering thought. Are we doing all we can to preserve the health of our childhood diabetics so that after twenty years of the disease they will be happy and healthy? I know I have not done enough. Of 249 cases in this group, after completing twenty years of the disease, only 30 per cent. are free from complications in the eyes, kidneys and heart. Again here, I care comparatively little about results in other clinics: what I want and my colleagues want is to improve the treatment of our own children. It is only fair to ourselves to point out that these 249 cases should represent the worst possible series of cases we shall ever report, because so many of them illustrate the results of treatment begun before the advent of insulin and all began it when diet was unnecessarily low in carbohydrate and calories. Although for the child diabetic the outlook for the second twenty years of diabetes is threatening, it should never be as bad as these early statistics imply.

There is not the slightest particle of doubt in my own mind that the diabetic child who has the greatest number of well-treated and honestly

at a fifth or even a tenth of the expense, and these are patients who yield dividends of health and efficiency. Only rarely is the complicated case, with, for instance, the loss of a leg, able to continue work, but the uncomplicated diabetic patient can be so protected that he or she is productive for years, is self-supporting, and can even contribute to the welfare of his diabetic ancestors. Education is necessary for all and preventive diabetic education for the relatives.

THE INDEPENDENCE OF DIABETICS

I have such faith in diabetics, such respect for them, that I believe they should be encouraged in every possible way to care for themselves. They are eager for independence and eager to contribute to better hospital facilities and to advance research in diabetes. They are so intelligent that they know it is to their advantage from every point of view to do so. I have concrete proof of this. The New England Deaconess Hospital, where in the George F. Baker Clinic many of my diabetics are treated, is planning an expansion. Our patients now occupy one-fourth of the beds and are to have that same proportion, 50 more, in the new construction, giving them 125 of the total 500 beds. To-day, 3,247 of them and their friends have contributed $290,000 towards the cost of these new beds, thereby exceeding their quota of $198,000. No other group at the Hospital has approached such an over-subscription of its assignment. And concurrently they have contributed to "The Diabetic Fund and Permanent Diabetic Fund", at the Boston Safe Deposit and Trust Company, to which 1,065 donations amounting to $123,384.37 have been sent. The income of such a Fund is small, but it represents a beginning. We would like a separate Clinical, Research and Teaching Unit at the Deaconess and we need a Diabetic Fund of $1,000,000 for research and for our camps for diabetic boys and girls, which this summer provided for 200 diabetic children. I would love to live to see both—the separate diabetic Clinical, Research and Teaching Unit established, and the Diabetic Fund grow to a million dollars, because I believe their creation here would lead to similar clinics and funds elsewhere in the world, just as The Diabetic Association in Great Britain has led to the development of our American Diabetes Association and many lay societies in the United States, and doubtless in other parts of the world as well.

Deaconess Hospital. The blood showed 129 mgm. glucose per 100 c.cm., CO_2 content 17 volumes per cent. (8 millimols per litre by the present terminology), and the next morning, when I reached the hospital, I found the patient happy and smiling.

Diabetes mellitus is hereditary and therefore at the present time there is a problem that did not exist a short time ago, i.e., the births of thousands of individuals hereditarily predisposed to the disease. The parents of these offspring are far too numerous and too healthy to prevent their having children. Therefore we are confronted to-day with a problem of diabetic heredity on so vast a scale that we must boldly face it.

THE EXPANDING NUMBER OF DIABETICS

The decrease in fatalities from diabetic coma, the lengthening lives of diabetics and the propagation of individuals with a diabetic heredity all lead to an increased and increasing number of diabetics to treat. Diabetes as a cause of death in the United States has already risen from twenty-seventh place in 1900 to eighth place in 1945, and if deaths from accidents are omitted, to seventh place. Soon it will pass tuberculosis and pneumonia, as it has already in various localities, so that only cancer and arteriosclerosis in its various sites in the brain, heart and kidneys will outrank it. The number of individuals requiring diabetic care is far greater than would be computed from reported deaths and duration. Half again as many of my patients die with the disease as are classified as dying from it. These figures are substantiated elsewhere, as demonstrated by my friend, Dr. Lester J. Palmer of the State of Washington. Then, too, there is the unrecognized diabetic. My own records, conservatively compiled, show that the disease has certainly been present for some five months before being diagnosed, as reckoned from the date of onset of early symptoms of the disease, and there must be many cases totally unrecognized.

More attention must be paid to diabetics. Not only should their growing number, which in my opinion certainly amounts to a million among our 140,000,000 population in the United States, be appreciated, but better facilities for their care must be adopted. Diabetes is a national problem. Already the United States Public Health Service has taken cognizance of it. Major Hugh L. C. Wilkerson and others of their Staff are familiarizing themselves with it here in Boston; they are also working with the Massa-chusetts Division of the Blind and the State Board of Health. The first survey is to determine the incidence of diabetes among the 6,400 blind in Massachusetts. Later I hope they will make an accurate survey of the existence of the disease in the 5,000 people of the town of Oxford, perhaps the first such survey ever to be conducted in the world. Greater provision for the care, the instruction and the prevention of diabetes should be made. For the complicated cases of diabetes more beds in hospitals are urgently required, but for the ambulatory case educational treatment can be provided

cases the disease has often been present for one, two or more years before it is diagnosed and, in consequence, serious complications may be present when the patient is first seen.

Treatment.—The obese type of diabetic is often relatively insulin-resistant but responds well to treatment by a low carbohydrate diet which reduces both the glycosuria and the weight. The diet should contain 80 to 120 gm. of carbohydrate and, if obesity is marked, the fat intake should be reduced to 50 gm. If the patient is not greatly overweight, protein and fat may be allowed in average helpings, and the carbohydrate evenly distributed throughout the day, 20 to 30 gm. being given at each meal. A convenient method of doing this is to give the patient a list of foods each of which contains 10 gm. of carbohydrate and is called one portion (one black line of Lawrence). The number of portions allowed at each meal can then be prescribed and the patient left to make his choice from the list. When serious complications, such as diabetic retinitis, are present it may be necessary to give insulin in order to obtain the best possible control of the diabetes, but in the absence of any such indication it is better, if possible, to avoid insulin as its use tends to result in a further increase in the patient's weight.

MODERATELY SEVERE DIABETICS

Under this heading will be included all diabetics who require insulin but whose disease cannot be considered as severe. With the exception of the mild cases already referred to, in which there is some special indication to give insulin, most of the cases in this group conform to a greater or lesser degree to the classical description in which thirst, polyuria, lassitude and loss of weight are the most typical symptoms. Treatment may conveniently be divided into two phases:—

(1) Stabilization.

(2) Maintenance.

Stabilization.—In the absence of ketosis the initial stabilization can usually be carried out quite satisfactorily without confining the patient to bed, in fact there is something to be said in favour of balancing diet and insulin under the normal conditions of the patient's everyday life. Against this advantage must be placed the longer time required to achieve the same degree of control as can be obtained in circumstances which allow of frequent urine tests and blood sugar estimations. In practice, the present shortage of beds makes it essential to be able to stabilize diabetics of moderate severity without admission to hospital; for this reason some simple methods of ambulatory treatment will be described in this section and stabilization in hospital considered subsequently under the heading of "severe diabetics".

In deciding whether or not a diabetic can safely be treated as an out-patient the most important single factor is the presence or absence of ketosis. Ambulatory treatment should, so far as possible, be reserved for those

THE TREATMENT OF DIABETES MELLITUS

By WILFRID OAKLEY, M.D., F.R.C.P.

Physician, Diabetic Department, King's College Hospital.

THERE is a natural tendency in therapeutics towards standardization, and the fact that insulin has an official dose of 5 to 100 units is an example of this tendency in the treatment of diabetes mellitus. In no disease, however, does treatment more need to be adapted to the individual or results more depend upon the appreciation of this fact by both doctor and patient.

For purposes of description it is, nevertheless, convenient to classify diabetics according to the severity of their disease in order that certain general principles of treatment may be laid down for each class. Severity is difficult to define in diabetes, as insulin requirement, which at first sight appears to be the obvious criterion, is apt to be misleading on account of the great individual variation in insulin sensitivity. A better appreciation of the meaning of severity can perhaps be obtained by a consideration of the length of time required for the development of ketosis in any diabetic under standard conditions of diet when insulin is withheld. By this definition the highly insulin-sensitive patient, who requires only a small dose of insulin but rapidly develops ketosis when insulin is stopped, is rightly considered a severe case, whilst the resistant case in which insulin requirement may be much larger but the liability to develop ketosis considerably less, must be looked upon as an essentially milder form of the disease. Adopting this definition of severity, diabetics will be subdivided into three main groups— mild, moderately severe and severe.

MILD DIABETICS

This group includes many early cases in which the disease process inevitably progresses until the patients become moderately severe or severe diabetics; these may properly be considered under the latter headings. The great majority of mild diabetics are elderly patients, more often women than men, who present a somewhat characteristic clinical picture which differs in certain important respects from that usually described in the textbooks and seen in younger and more severe cases. These elderly mild cases are often obese individuals, the distribution of fat being suggestive of pituitary dysfunction, they seldom complain of much thirst and rarely develop ketosis. With the exception of pruritus vulvæ in women, symptoms directly referable to hyperglycæmia and glycosuria are remarkable for their absence, diabetes being diagnosed as a result of routine examination of the urine or the occurrence of some complication, such as failing vision due to retinitis, neuritis or gangrene. Owing to the insidious nature of the onset in these

cases the disease has often been present for one, two or more years before it is diagnosed and, in consequence, serious complications may be present when the patient is first seen.

Treatment.—The obese type of diabetic is often relatively insulin-resistant but responds well to treatment by a low carbohydrate diet which reduces both the glycosuria and the weight. The diet should contain 80 to 120 gm. of carbohydrate and, if obesity is marked, the fat intake should be reduced to 50 gm. If the patient is not greatly overweight, protein and fat may be allowed in average helpings, and the carbohydrate evenly distributed throughout the day, 20 to 30 gm. being given at each meal. A convenient method of doing this is to give the patient a list of foods each of which contains 10 gm. of carbohydrate and is called one portion (one black line of Lawrence). The number of portions allowed at each meal can then be prescribed and the patient left to make his choice from the list. When serious complications, such as diabetic retinitis, are present it may be necessary to give insulin in order to obtain the best possible control of the diabetes, but in the absence of any such indication it is better, if possible, to avoid insulin as its use tends to result in a further increase in the patient's weight.

MODERATELY SEVERE DIABETICS

Under this heading will be included all diabetics who require insulin but whose disease cannot be considered as severe. With the exception of the mild cases already referred to, in which there is some special indication to give insulin, most of the cases in this group conform to a greater or lesser degree to the classical description in which thirst, polyuria, lassitude and loss of weight are the most typical symptoms. Treatment may conveniently be divided into two phases:—

(1) Stabilization.

(2) Maintenance.

Stabilization.—In the absence of ketosis the initial stabilization can usually be carried out quite satisfactorily without confining the patient to bed, in fact there is something to be said in favour of balancing diet and insulin under the normal conditions of the patient's everyday life. Against this advantage must be placed the longer time required to achieve the same degree of control as can be obtained in circumstances which allow of frequent urine tests and blood sugar estimations. In practice, the present shortage of beds makes it essential to be able to stabilize diabetics of moderate severity without admission to hospital; for this reason some simple methods of ambulatory treatment will be described in this section and stabilization in hospital considered subsequently under the heading of "severe diabetics".

In deciding whether or not a diabetic can safely be treated as an out-patient the most important single factor is the presence or absence of ketosis. Ambulatory treatment should, so far as possible, be reserved for those

THE TREATMENT OF DIABETES MELLITUS

By WILFRID OAKLEY, M.D., F.R.C.P.

Physician, Diabetic Department, King's College Hospital.

THERE is a natural tendency in therapeutics towards standardization, and the fact that insulin has an official dose of 5 to 100 units is an example of this tendency in the treatment of diabetes mellitus. In no disease, however, does treatment more need to be adapted to the individual or results more depend upon the appreciation of this fact by both doctor and patient.

For purposes of description it is, nevertheless, convenient to classify diabetics according to the severity of their disease in order that certain general principles of treatment may be laid down for each class. Severity is difficult to define in diabetes, as insulin *requirement*, which at first sight appears to be the obvious criterion, is apt to be misleading on account of the great individual variation in insulin sensitivity. A better appreciation of the meaning of severity can perhaps be obtained by a consideration of the length of time required for the development of ketosis in any diabetic under standard conditions of diet when insulin is withheld. By this definition the highly insulin-sensitive patient, who requires only a small dose of insulin but rapidly develops ketosis when insulin is stopped, is rightly considered a severe case, whilst the resistant case in which insulin requirement may be much larger but the liability to develop ketosis considerably less, must be looked upon as an essentially milder form of the disease. Adopting this definition of severity, diabetics will be subdivided into three main groups—mild, moderately severe and severe.

MILD DIABETICS

This group includes many early cases in which the disease process inevitably progresses until the patients become moderately severe or severe diabetics; these may properly be considered under the latter headings. The great majority of mild diabetics are elderly patients, more often women than men, who present a somewhat characteristic clinical picture which differs in certain important respects from that usually described in the textbooks and seen in younger and more severe cases. These elderly mild cases are often obese individuals, the distribution of fat being suggestive of pituitary dysfunction, they seldom complain of much thirst and rarely develop ketosis. With the exception of pruritus vulvæ in women, symptoms directly referable to hyperglycæmia and glycosuria are remarkable for their absence, diabetes being diagnosed as a result of routine examination of the urine or the occurrence of some complication, such as failing vision due to retinitis, neuritis or gangrene. Owing to the insidious nature of the onset in these

morning, but some diabetics, especially those whose work necessitates much physical exertion, require the smaller dose in the morning.

The chief difficulty likely to be encountered in this method of treatment is the presence of a lowered renal threshold; this should be suspected when satisfactory clinical improvement and repeatedly normal blood sugars are associated with persistent heavy glycosuria. If this occurs a specimen should be tested half an hour before and another half an hour after the noon blood sugar, in order to determine the approximate level of blood sugar at which sugar appears in the urine. If this procedure is adopted whenever a blood sugar is taken the required information will usually soon be obtained. If the threshold is not below 150 mgm. per cent. it is safe to aim at keeping the second noon specimen green with Benedict's solution, but in those cases in which it is very low, 100 mgm. per cent. or less, no reliance should be placed on the results of tests with qualitative Benedict's solution, treatment being based on Rothera's test for diacetic acid and blood sugar estimations.

When the case is considered suitable for a single injection of P.Z.I., alone or with S.I., the diet must be arranged so that the carbohydrate is more evenly distributed throughout the day, the amounts allowed at tea and the evening meal being about the same and rather less than those given at breakfast and lunch; a bedtime feed of 15 to 20 gm. should be taken by all diabetics on P.Z.I. to minimize the risk of nocturnal hypoglycæmia. The initial dose of P.Z.I. should be 12 to 16 units, and in view of its cumulative action this should not be increased for at least two days. The dose should then be adjusted from the result of the second morning test and, if necessary, increased by 4 units every third day until this test is sugar-free or nearly so. At this stage the noon blood sugar should be estimated to determine whether or not the patient needs a mixed dose. If the blood sugar is less than 180 mgm. per cent. and the clinical condition, including weight, is satisfactory, there is no need to give S.I., but if this figure is exceeded on two consecutive occasions better control can only be obtained by adding S.I. to the morning injection. Any attempt to lower this figure when the second morning specimen is sugar-free, by giving more P.Z.I., is likely to result in severe nocturnal hypoglycæmia. In order to avoid the risk of inactivitating the acid S.I. by the introduction of buffered P.Z.I., the former should be introduced into the syringe first, a little air having previously been injected into the protamine bottle. The mixing of S.I. and P.Z.I. in the same syringe, on account of the excess of protamine present in the latter, results in the conversion of some of the S.I. into P.Z.I., and allowance should be made for this. In practice the best way of so doing is to keep the dose of S.I. as large and that of P.Z.I. as small as possible, the size of the former being assessed from the noon blood sugar and that of the latter from the second morning specimen. Most diabetics on a mixed dose of this kind tend to show sugar in the urine between 6 and 10 p.m. but, unless this

diabetics in whom ketosis, as judged by Rothera's test, is absent or slight, and such treatment is likely to give the best results in patients with intelligence and favourable home conditions.

Assessment of insulin dosage.—Before treatment is started the patient should be weighed and the blood sugar estimated at about noon; this is a convenient time and the result approximates to the fasting level. A diet containing 150 gm. of carbohydrate is prescribed for a week, at the end of which time the patient is again weighed, night and morning specimens of urine are tested for sugar and acetone bodies, and the noon blood sugar estimation is repeated. From the results obtained it is usually possible to decide whether or not insulin is necessary and, if so, the best type and initial dosage. The measure of success achieved in making this decision depends to a large extent upon experience, but satisfactory results can be obtained in most cases if the following procedure is adopted. In the first place it is important to decide whether to start treatment with two injections of soluble insulin (S.I.) or a single injection of protamine zinc insulin (P.Z.I.); this will depend upon the age, mentality, occupation and intelligence of the patient. For young children and those dependent upon others to give their insulin, a single injection method has obvious advantages and should be tried first; the same applies to those patients who for any reason are strongly opposed to taking insulin at all. Occupation is also a factor to be considered, as P.Z.I. alone or in combination with S.I. is better suited for those whose work allows of regular meals than those in whom shift work or some other cause of variation in the daily routine makes regular meals impossible. Intelligence should be assessed when prescribing mixed doses, as the technique of administration and adjustment is more difficult than with two doses of S.I. If morning and evening injections of S.I. are used the diet should be arranged so as to give the largest amount of carbohydrate at breakfast and the evening meal, and a buffer of 15 to 20 gm. of carbohydrate put in at 11 a.m. to prevent hypoglycæmia before lunch. It is usually safe to start with 12 to 16 units in the morning and 4 units less at night and increase each dose by 4 units twice a week until the early morning and midday specimens of urine show only traces of sugar (the bladder should be emptied about an hour before, so as to eliminate any urine which may contain sugar from the previous meal); these specimens will be referred to respectively as the second morning and second noon specimens. As the duration of the hypoglycæmic action of insulin is in direct proportion to the size of the dose it is often better, when this exceeds 40 units, to adjust the morning insulin from the urine test made before tea or the evening meal. When the dose of insulin, as judged by these tests, is thought to be approximately corrected, the noon blood sugar estimation should be repeated and the morning insulin adjusted so as to give a figure of between 100 and 150 mgm. per cent., the higher figure being the safer when the dose exceeds 30 units. The evening insulin should usually be kept to 4 to 8 units less than the

Two additional arrangements of insulin are of particular value in the treatment of severe diabetics. The tendency for diabetics on a mixed dose to relapse in the evening has already been mentioned, and in severe cases this relapse may have to be prevented if the control of the disease is to be maintained. This can be done by giving a dose of soluble insulin before the evening meal or better still before tea; the earlier it is given the more effective it is in preventing the relapse and the less danger there is of it producing hypoglycæmia during the night. The second arrangement probably gives the best control possible in most very severe diabetics and consists of an injection of S.I. in the morning and of a mixed dose of S.I. and P.Z.I. before tea or the evening meal; here again the earlier it is given the better. This type of treatment is particularly suitable for those diabetics who, when given two doses of S.I., tend to relapse during the night and start the day with severe ketosis and a high fasting blood sugar. The addition of a small dose of P.Z.I. to the evening S.I. will usually prevent morning ketosis, and help to control the fasting blood sugar. The dose of P.Z.I. should be kept as small as possible so as not to make the fasting blood sugar so low that insufficient S.I. can be given to act throughout the day without producing severe hypoglycæmia during the morning.

Maintenance.—When stabilization is carried out in hospital there is apt to be something of a dividing line between it and maintenance. This is due to the fact that in hospital, diabetics are balanced under conditions which differ greatly from those under which they normally live and work. The greater physical activity of normal life is apt to result in severe hypoglycæmic attacks if this fact is not remembered and the dose of insulin suitably reduced to allow for it. In other respects the maintenance of severe diabetics differs in no way from that of less severe cases except in the greater difficulties the former may experience in steering a middle course between hyper- and hypo-glycæmia.

No mention has been made of globin insulin because, in my experience, it is generally less satisfactory for single injection than P.Z.I., and too little is yet known of the action of mixed doses of globin and S.I. or P.Z.I. to justify a description of their use in an article of this nature.

INTERCURRENT INFECTION IN DIABETICS

During minor infective ailments, such as the common cold, it is usually sufficient to increase the dose of insulin by about 5 units, but for more severe conditions, such as gastro-enteritis, more drastic changes in treatment may be required. If for any reason the normal diet cannot be taken, the patient should eat the carbohydrate portion only in the form of milk or fruit drinks, bread and milk, or dry toast, and inject the full amount of insulin; if vomiting prevents even carbohydrate food from being retained, half the normal dose of insulin should be given without food and the urine tested frequently for acetone bodies.

relapse is severe and associated with ketosis or a return of diabetic symptoms, it can safely be ignored.

Maintenance.—When treatment is ambulatory there is no dividing line between stabilization and maintenance, such as tends to exist when the former is carried out in hospital. All reasonably intelligent diabetics should be taught to test their urine for sugar and adjust their insulin from the results obtained. The symptoms of hypoglycæmia, its prevention and treatment, should be explained fully to the patient and the importance of regular visits to his doctor or a hospital diabetic clinic impressed upon him. Education in the proper care of the feet plays a large part in the prevention of sepsis and infected gangrene, especially in elderly diabetics, the proper treatment of callosities and corns being of particular importance in this connexion.

SEVERE DIABETICS

For convenience of description only those diabetics whose urine contains acetone bodies in sufficient quantity to make hospital treatment desirable, if not absolutely necessary, will be considered under this heading.

Stabilization.—The treatment of these so-called severe cases is essentially the same as that already described but, being more urgent, must be more quickly and effectively applied. This is made possible in hospital by frequent urine tests and blood sugar estimations, which enable relatively large doses of insulin to be given with safety in the early stages of treatment. As a rule it is best to start with two or more doses of S.I. and, if desirable, to change over to a mixed dose when the diabetes has been reasonably well controlled. The chief advantages of this method are its simplicity and the rapidity with which it removes ketosis and relieves thirst and polyuria; in addition, if the requirement of S.I. is determined before the change over to a mixed dose is made, it is always possible, should treatment by a single injection prove unsatisfactory, to return without waste of time to two injections of S.I.

When very severe ketosis is present soluble insulin should always be used and given four-hourly or six-hourly according to the severity of the condition. Diet should consist of two-hourly feeds of 20 gm. of carbohydrate in the form of milk drinks, bread and milk, milk pudding, or fruit juice sweetened with glucose. The dosage of insulin is best assessed in the early stages by blood sugar determinations, but can be adjusted from four-hourly urine tests, 28 to 40 units being given for a red test, 16 to 24 for a yellow or thick green, and 0 to 12 for a clear green or blue. As soon as ketosis has disappeared the feeds may be given four-hourly and later rearranged into meals; at the same time the number of injections can be reduced to morning, midday and evening, the midday being the last to stop. The prompt institution of this form of treatment in cases of very severe ketosis will almost invariably prevent the onset of diabetic coma.

Two additional arrangements of insulin are of particular value in the treatment of severe diabetics. The tendency for diabetics on a mixed dose to relapse in the evening has already been mentioned, and in severe cases this relapse may have to be prevented if the control of the disease is to be maintained. This can be done by giving a dose of soluble insulin before the evening meal or better still before tea; the earlier it is given the more effective it is in preventing the relapse and the less danger there is of it producing hypoglycæmia during the night. The second arrangement probably gives the best control possible in most very severe diabetics and consists of an injection of S.I. in the morning and of a mixed dose of S.I. and P.Z.I. before tea or the evening meal; here again the earlier it is given the better. This type of treatment is particularly suitable for those diabetics who, when given two doses of S.I., tend to relapse during the night and start the day with severe ketosis and a high fasting blood sugar. The addition of a small dose of P.Z.I. to the evening S.I. will usually prevent morning ketosis, and help to control the fasting blood sugar. The dose of P.Z.I. should be kept as small as possible so as not to make the fasting blood sugar so low that insufficient S.I. can be given to act throughout the day without producing severe hypoglycæmia during the morning.

Maintenance.—When stabilization is carried out in hospital there is apt to be something of a dividing line between it and maintenance. This is due to the fact that in hospital, diabetics are balanced under conditions which differ greatly from those under which they normally live and work. The greater physical activity of normal life is apt to result in severe hypoglycæmic attacks if this fact is not remembered and the dose of insulin suitably reduced to allow for it. In other respects the maintenance of severe diabetics differs in no way from that of less severe cases except in the greater difficulties the former may experience in steering a middle course between hyper- and hypo-glycæmia.

No mention has been made of globin insulin because, in my experience, it is generally less satisfactory for single injection than P.Z.I., and too little is yet known of the action of mixed doses of globin and S.I. or P.Z.I. to justify a description of their use in an article of this nature.

INTERCURRENT INFECTION IN DIABETICS

During minor infective ailments, such as the common cold, it is usually sufficient to increase the dose of insulin by about 5 units, but for more severe conditions, such as gastro-enteritis, more drastic changes in treatment may be required. If for any reason the normal diet cannot be taken, the patient should eat the carbohydrate portion only in the form of milk or fruit drinks, bread and milk, or dry toast, and inject the full amount of insulin; if vomiting prevents even carbohydrate food from being retained, half the normal dose of insulin should be given without food and the urine tested frequently for acetone bodies.

DIABETIC COMA

By GEORGE GRAHAM, M.D., F.R.C.P.

Emeritus Physician, St. Bartholomew's Hospital.

DIABETIC coma, before the introduction of insulin, was a most dreaded and fatal complication. Nowadays it is rarely seen and should never occur in an established case. If it does, either the patient has failed to follow out instructions or the medical attendant has not given enough insulin.

Coma may occasionally occur if the disease is very severe. The patient may have been apparently well a few days before, and the practitioner may not be called in until the patient is in coma. A much more common cause is the onset of an acute infection. This may be so severe that the patient may develop coma very quickly in spite of having insulin, but the bad mistake is sometimes made of omitting the insulin because the patient is vomiting.

PREVENTION

The best way of preventing the onset of coma is to make the diagnosis of impending coma as early as possible and to treat the condition at once with adequate doses of insulin and glucose.

If a patient who is taking, say 40 units of the soluble quick-acting insulin in the morning and 24 units at night, is taken seriously ill during the night, the following procedure should be adopted. Provided that the ordinary amount of carbohydrate is taken at breakfast, the morning dose of insulin should be taken as usual. If the patient is very ill, and vomiting, he is inclined to omit the insulin as he cannot take food, whereas it is vitally important to give it. The urine passed at, say 8 a.m., should be tested, and if sugar is absent half the usual dose of insulin is given, but if the test is red or yellow the full dose of insulin should be given. The urine should be tested every three hours, and if the urine four to six hours after the morning insulin gives a red or yellow test with Benedict's solution, more insulin should be given at once, say half the morning dose, but if it is green or blue, insulin should not be given. The urine is again collected every three hours and if the urine in the next four- to six-hour period is red or yellow the same dose of soluble insulin as in the morning should be given, but none if the test is green or blue. This procedure is continued and it is usually possible to increase the dose of insulin sufficiently to prevent the onset of coma.

Many patients have a mixture of the soluble quick-acting insulin (say 40 units), with either the milky slow-acting protamine zinc insulin or the clear slow-acting globin insulin (say 20 units), and a slightly different procedure is followed. If the patient can eat his breakfast the same dose should be given and the urine collected as before in the three-hourly periods. If the test in the four- to six-hour period is red or yellow, half the dose of soluble insulin

should be given and the urine collected again. If the urine in the next four- to six-hour period gives a red or yellow test, more insulin is needed, but the protamine zinc insulin is beginning to work by this time and it is wiser not to give insulin but to wait for the result of the next four- to six-hour period. If this is red or yellow (say at 2 a.m.), half the morning dose of soluble insulin should be given. If the patient still has fever the next morning it is wiser to give the soluble insulin without the slow-acting insulin and proceed as described in the preceding paragraph.

The dose of insulin is more difficult to adjust when patients are taking big doses of the slow-acting protamine zinc or globin insulin, and little or no quick-acting insulin. Thus, if say 40 units of the protamine zinc or globin insulin mixed with 10 units only of the soluble insulin are given at 8 a.m. on the first day of the illness, a different procedure should be adopted. If the urine in the four- to six-hour period, i.e. 2 p.m., shows a red or yellow test, the same dose of soluble insulin should be given but none if the test is green or blue. In the second four- to six-hour period a red or yellow test means that more insulin is needed (8 p.m.). This is the time that the protamine zinc or globin insulin is active and it is probably safer, unless the patient is very ill, not to give any insulin at this time. But if the third four- to six-hour period again gives a red or yellow test (2 a.m.), some soluble insulin should be given, say 10 to 20 units. The next morning at 8 a.m., if a red or yellow test is found the protamine zinc or globin insulin should not be given. The total dose of insulin given on the first day of illness was 40 units of protamine zinc or globin, and 10+10+10 units of soluble insulin, making 70 units in all. Half of this dose of soluble insulin should be given and the subsequent doses arranged as in the case of the patient taking soluble insulin. An aggravating complication is the inability of the patient to take ordinary food because of nausea and vomiting. This can often be overcome by giving lactose or glucose dissolved in water and flavoured with orange, lemon or some other fruit juice. At least 50 gm. (2 ounces of glucose) should be given every six hours. If the patient vomits these drinks the glucose must be given in the form of an intravenous drip of 10 per cent. glucose solution, and 2,400 to 3,000 c.cm., i.e. 240 to 300 gm. of glucose, may be given in the day, if necessary.

DIAGNOSIS

If the patient has not been treated efficiently he may first be seen in coma. In this condition the patient may be deeply comatose or may be easily roused if the condition is not far advanced. The patient's breath smells strongly of acetone and, if the practitioner knows that he can detect this smell, it is a most useful aid to diagnosis. Some people know that they are unable to recognize it and use the other signs and tests. Others, unfortunately, have not learnt that they cannot recognize the smell and are apt to say that the patient is not in diabetic coma because there is no smell

of acetone in the breath. The breathing of the diabetic (air hunger) is very characteristic, as it is deep and slow and the depth is recognized by the movements of the abdomen. In the pre-comatose condition the patient may be breathing twice as deeply, and in deep coma four or five times as deeply. The skin is dry and the tongue and mouth are also dry. The tension of the eyeballs is much reduced and is diagnostic, since this does not occur in any other disease so long as the patient is alive. The urine will always contain much sugar and, with rare exceptions, an excess of acetone bodies. The blood sugar is nearly always very high.

The *differential diagnosis* is from coma due to hypoglycæmia. In this condition the breath does not smell of acetone and the breathing is shallow, so that the abdomen hardly moves at all. The skin is moist and often sweating profusely. The eyeball tension is normal or even slightly raised. The urine may contain sugar and even some acetone bodies, if the bladder has not been emptied for some hours; the blood sugar is below 50 mgm. per 100 c.cm.

TREATMENT

The essentials of treatment of diabetic coma are three in number: (1) supply plenty of fluid to the dehydrated patient; (2) give plenty of insulin; (3) make certain that the patient has enough sugar in his body while the poisonous aceto-acetic acid is being destroyed in the tissues.

Fluids.—If the patient can swallow he should be given 300 c.cm. of a 10 per cent. glucose solution made with water or ½ normal physiological saline every three hours; this will supply about 2,400 c.cm. of fluid in the day, and 240 gm. of glucose. If he cannot swallow, it can be given by a nasal catheter directly into the stomach, but it is better to give it by means of an intravenous drip, 10 per cent. glucose in ⅛ normal physiological saline. It is wise to give between 2,400 and 3,000 c.cm. of fluid in the twenty-four hours, as the blood volume may have become very concentrated and the hæmoglobin percentage may be 110 per cent. or more.

The *dose of insulin* depends upon two factors: (a) how much insulin the patient has been having, and (b) the depth of the coma. If he has needed 200 units a day, it is useless to start off with an initial dose of 50 units, whereas if the dose has been 20 units daily a dose of 50 units may be adequate. If the usual dosage is not known it is most important to know the amount of sugar in the blood and, if this is very high, over 400 mgm. per 100 c.cm., 100 units should be given. If the blood sugar is not known the initial dose should be 50 units more than the usual morning dose, and the subsequent dosage determined by the result of the urine tests. If neither the usual dosage nor the blood sugar is known the initial dose should be at least 100 units. An initial dose of 50 units should be given as soon as the diagnosis is made without waiting for the result of the blood sugar estimation. In the absence of blood sugar estimations, the urine must be collected and this is best done by passing a self-retaining catheter. It is important to connect this with a Duke's apparatus to prevent the risk of a

urinary infection developing. The urine should be tested hourly. The blood pressure must be estimated, and if it is very low, less than 100 mm. Hg systolic, the prognosis is very bad.

As soon as the blood has been collected for the estimation of its sugar content (if this is possible) at least 50 gm. (2 oz.) of glucose should be given either by mouth, by nasal catheter, or by intravenous drip, and the insulin given subcutaneously or, if the patient is very ill, intravenously. It is better to wait three hours before giving any more insulin, and if the patient is still deeply comatose, 100 units should be given together with another 50 gm. of glucose by mouth or nasal catheter, if an intravenous glucose drip is not being administered. If after another three hours the patient still shows no signs of improvement, the dose of insulin should be increased by one-half, and another 50 gm. of glucose given, and this procedure repeated every three hours. In these very ill patients the blood pressure is always low, and 15 mgm. of desoxycorticosterone should be given on admission and repeated after three or six hours. Unless the patient shows signs of recovery after nine hours it is unlikely that he will recover.

If the patient has begun to improve after three hours, insulin should not be given until the result of the urine test on the period five to six hours is known. If this test is red by Benedict's test, the initial dose should be increased by one half, i.e. 50 units is followed by 75 and 100 units, followed by 150 units; if the test is yellow the initial dosage should be repeated; if the test is green or blue, insulin should not be given, but 25 gm. of glucose is given to prevent the risk of hypoglycæmia. If insulin has been given, after six hours the same procedure is repeated and the further dosage of sugar and insulin determined on the same principles, with the insulin dosage either increased by one-half if the test is red, kept at the same amount for yellow tests, and not given if the tests are green or blue, until the test becomes red or yellow again, when half the previous dose should be given. The patient should be conscious by six to twelve hours if this procedure is adopted, and the ketones will have nearly all disappeared.

A few patients die in spite of this treatment, but these have usually been in coma for some hours before adequate treatment is started or have developed a severe infection. A careful watch must be kept for the symptoms of hypoglycæmia, and if a patient who has recovered consciousness relapses into coma again, glucose, 25 gm., should be given intravenously without delay.

As soon as the patient has recovered from shock a careful search should be made for the physical signs of any infection and the appropriate treatment, medical or surgical, instituted as soon as possible.

The subsequent task of ascertaining the correct dose of insulin is sometimes very difficult. The urine must be tested every three hours and the blood sugar estimated two or three times a day, if possible.

of acetone in the breath. The breathing of the diabetic (air hunger) is very characteristic, as it is deep and slow and the depth is recognized by the movements of the abdomen. In the pre-comatose condition the patient may be breathing twice as deeply, and in deep coma four or five times as deeply. The skin is dry and the tongue and mouth are also dry. The tension of the eyeballs is much reduced and is diagnostic, since this does not occur in any other disease so long as the patient is alive. The urine will always contain much sugar and, with rare exceptions, an excess of acetone bodies. The blood sugar is nearly always very high.

The *differential diagnosis* is from coma due to hypoglycæmia. In this condition the breath does not smell of acetone and the breathing is shallow, so that the abdomen hardly moves at all. The skin is moist and often sweating profusely. The eyeball tension is normal or even slightly raised. The urine may contain sugar and even some acetone bodies, if the bladder has not been emptied for some hours; the blood sugar is below 50 mgm. per 100 c.cm.

TREATMENT

The essentials of treatment of diabetic coma are three in number: (1) supply plenty of fluid to the dehydrated patient; (2) give plenty of insulin; (3) make certain that the patient has enough sugar in his body while the poisonous aceto-acetic acid is being destroyed in the tissues.

Fluids.—If the patient can swallow he should be given 300 c.cm. of a 10 per cent. glucose solution made with water or ⅓ normal physiological saline every three hours; this will supply about 2,400 c.cm. of fluid in the day, and 240 gm. of glucose. If he cannot swallow, it can be given by a nasal catheter directly into the stomach, but it is better to give it by means of an intravenous drip, 10 per cent. glucose in ⅓ normal physiological saline. It is wise to give between 2,400 and 3,000 c.cm. of fluid in the twenty-four hours, as the blood volume may have become very concentrated and the hæmoglobin percentage may be 110 per cent. or more.

The *dose of insulin* depends upon two factors: (a) how much insulin the patient has been having, and (b) the depth of the coma. If he has needed 200 units a day, it is useless to start off with an initial dose of 50 units, whereas if the dose has been 20 units daily a dose of 50 units may be adequate. If the usual dosage is not known it is most important to know the amount of sugar in the blood and, if this is very high, over 400 mgm. per 100 c.cm., 100 units should be given. If the blood sugar is not known the initial dose should be 50 units more than the usual morning dose, and the subsequent dosage determined by the result of the urine tests. If neither the usual dosage nor the blood sugar is known the initial dose should be at least 100 units. An initial dose of 50 units should be given as soon as the diagnosis is made without waiting for the result of the blood sugar estimation. In the absence of blood sugar estimations, the urine must be collected and this is best done by passing a self-retaining catheter. It is important to connect this with a Duke's apparatus to prevent the risk of a

poured together, and just boiled again in the flame. If reduction takes place on standing for two minutes the probability is that the reducing substance is glucose. High concentrations of sugar are practically always diabetic in origin. If the specific gravity of the urine is above 1020 and obvious reduction is present, the reducing substance is nearly always glucose. If the specific gravity is above 1025 and the reduction is doubtful, the reducing substances are usually normal constituents in high concentration.

Of the less usual sugars, lactose most commonly occurs but is found only during pregnancy, rarely earlier than the second trimester, and during lactation. Even during pregnancy it is more common to find glucose in the urine than lactose: the result of temporary renal glycosuria of pregnancy. Lactose is easily recognized by the fact that it does not ferment with yeast, provided the specimen of urine is fresh and boiled before fermentation to avoid the effect of lactose fermenting organisms. When sugar is found in the urine during pregnancy it is always advisable to estimate the blood sugar. If the fasting level of the blood sugar is normal the condition need only be watched until labour is past, and no special precautions are necessary. It is usually unnecessary to investigate the presence of the more unusual sugars, except when glycosuria is discovered which cannot easily be explained by any other means. Lævulose and galactose may occur quite frequently in the urine in hospital patients, since these sugars may be administered for hepatic function tests. Pentosuria is rare but may occur during the fruit seasons from pentose in the prunus fruits. Exton (1936), found that in 97 per cent. of patients with glycosuria the reduction was due to glucose if the amount of sugar exceeded 1 per cent., whilst other substances accounted for 40 per cent. of reductions in lower concentrations of reducing substances.

The amount of sugar in the urine is to some extent significant. Values of over 2 per cent. glucose are nearly always due to diabetes mellitus. The patient with renal glycosuria seldom passes more than 1.5 per cent. of sugar in the urine, even after test doses of glucose, whilst the total quantity of sugar passed in the urine per day in renal glycosuria seldom exceeds 20 gm. (Finley and Rabinowitch, 1923-24). In the diabetic it is common for amounts over 100 gm. of glucose to be lost in the urine before treatment is instituted.

THE BLOOD SUGAR

The ultimate diagnosis of diabetes rests on finding elevation of the blood sugar. For this purpose a single sample of blood may be sufficient, showing a level above 120 mgm. per cent. fasting, or above 180 mgm. per cent. at any time in the day in relation to meals. The higher the value of the blood sugar, the more certainty there is of the diagnosis of diabetes. For example, in a female patient aged fifty years suffering from frequency of micturition, pruritus and glycosuria, a blood sugar value of 360 mgm. per cent. is diagnostic of diabetes. Or in a young male patient, emaciated, thirsty, dehydrated, with glucose and acetone in the urine, a blood sugar value of 420 mgm. per cent. is diagnostic of diabetes with incipient coma. Apart from any academic investigations which might be justified in such instances, treatment of the diabetic state should be started immediately.

THE LABORATORY DIAGNOSIS OF DIABETES MELLITUS

By ALEXANDER LYALL, M.D., F.R.C.P.

Clinical Chemist, Aberdeen Royal Infirmary.

THE diagnosis of diabetes mellitus may be practically certain from the clinical observations on an individual with thirst, polyuria, loss of strength, pruritus, glycosuria and ketonuria but can be absolute only on recognition of elevation of the blood sugar, since any of these cardinal symptoms may occur in other conditions. Thirst can occur in febrile and hysterical states, in certain generalized diseases of the skeleton, such as myelomatosis, and in diabetes insipidus. Polyuria occurs in chronic nephritis, hysterical states, diabetes insipidus and in abnormalities of the urinary tract. Loss of weight and strength are common in many other states, chiefly in malignant conditions and in pulmonary tuberculosis, whilst on the other hand the diabetic, especially in the later decades, is frequently obese. Pruritus is a common complaint in local pelvic conditions, especially about the menopause when the incidence of diabetes is high. Glycosuria is found in many conditions other than in diabetes, including renal glycosuria, endocrine dyscrasias, severe injuries, head injuries, cerebral hæmorrhage, severe or widespread sepsis, carbon monoxide poisoning, and after ingestion of drugs or after anæsthesia. Ketonuria occurs in many states other than in diabetes: in hyperemesis gravidarum, in relative starvation before or after abdominal operations, and in severe thyrotoxicosis. Glycosuria and ketonuria rarely occur together except in diabetes mellitus. The exceptions are when a pre-existent ketosis is being treated by massive ingestion of glucose: until the ketosis is overcome both sugar and acetone may be found in the urine for thirty-six to forty-eight hours.

The practitioner may discover a reducing substance in the urine accidently in a routine examination, or he may have his suspicions aroused by symptomatology or clinical observation that diabetes may be present and have his suspicion confirmed by finding sugar in the urine. In the former instance the probability is 10 to 1 against the patient having diabetes: in the latter instance the probability is reversed.

REDUCING SUBSTANCES IN THE URINE

Reducing substances which may occur in the urine include dextrose, lactose, lævulose, galactose, pentose, some drugs, including rhubarb, senna, amidopyrine, ascorbic acid, and high concentrations of normal urinary constituents, including creatinine, uric acid, glycuronates or abnormal metabolic urinary constituents, such as homogentisic acid. Test solutions most commonly in use are Benedict's and Fehling's solutions; the latter should be freshly prepared weekly.

Equal quantities of Fehling's solution and urine are boiled in two test tubes,

poured together, and just boiled again in the flame. If reduction takes place on standing for two minutes the probability is that the reducing substance is glucose. High concentrations of sugar are practically always diabetic in origin. If the specific gravity of the urine is above 1020 and obvious reduction is present, the reducing substance is nearly always glucose. If the specific gravity is above 1025 and the reduction is doubtful, the reducing substances are usually normal constituents in high concentration.

Of the less usual sugars, lactose most commonly occurs but is found only during pregnancy, rarely earlier than the second trimester, and during lactation. Even during pregnancy it is more common to find glucose in the urine than lactose: the result of temporary renal glycosuria of pregnancy. Lactose is easily recognized by the fact that it does not ferment with yeast, provided the specimen of urine is fresh and boiled before fermentation to avoid the effect of lactose fermenting organisms. When sugar is found in the urine during pregnancy it is always advisable to estimate the blood sugar. If the fasting level of the blood sugar is normal the condition need only be watched until labour is past, and no special precautions are necessary. It is usually unnecessary to investigate the presence of the more unusual sugars, except when glycosuria is discovered which cannot easily be explained by any other means. Lævulose and galactose may occur quite frequently in the urine in hospital patients, since these sugars may be administered for hepatic function tests. Pentosuria is rare but may occur during the fruit seasons from pentose in the prunus fruits. Exton (1936), found that in 97 per cent. of patients with glycosuria the reduction was due to glucose if the amount of sugar exceeded 1 per cent., whilst other substances accounted for 40 per cent. of reductions in lower concentrations of reducing substances.

The amount of sugar in the urine is to some extent significant. Values of over 2 per cent. glucose are nearly always due to diabetes mellitus. The patient with renal glycosuria seldom passes more than 1.5 per cent. of sugar in the urine, even after test doses of glucose, whilst the total quantity of sugar passed in the urine per day in renal glycosuria seldom exceeds 20 gm. (Finley and Rabinowitch, 1923-24). In the diabetic it is common for amounts over 100 gm. of glucose to be lost in the urine before treatment is instituted.

THE BLOOD SUGAR

The ultimate diagnosis of diabetes rests on finding elevation of the blood sugar. For this purpose a single sample of blood may be sufficient, showing a level above 120 mgm. per cent. fasting, or above 180 mgm. per cent. at any time in the day in relation to meals. The higher the value of the blood sugar, the more certainty there is of the diagnosis of diabetes. For example, in a female patient aged fifty years suffering from frequency of micturition, pruritus and glycosuria, a blood sugar value of 360 mgm. per cent. is diagnostic of diabetes. Or in a young male patient, emaciated, thirsty, dehydrated, with glucose and acetone in the urine, a blood sugar value of 420 mgm. per cent. is diagnostic of diabetes with incipient coma. Apart from any academic investigations which might be justified in such instances, treatment of the diabetic state should be started immediately.

In most cases of glycosuria discovered during medical examinations for the Services or for life insurance, or discovered in routine medical examinations following other complications, e.g. sciatica, failing eyesight, boils, it is essential to carry out a sugar tolerance test to clarify the position.

The patient receives no food after 8 o'clock on the evening before the test. Next morning the overnight sample of urine is collected, say at 7 a.m. Urine is again passed before the test; this provides a true fasting sample of urine at 9 a.m. which is useful. If this contains sugar the condition is probably diabetes mellitus, since the majority of cases of renal glycosuria pass urine which is free of sugar in the fasting state. A sample of venous blood is taken and the patient is given 50 gm. of glucose dissolved in 3 ounces (85 c.cm.) of water. Care should be taken that no sugar is spilled over the person or over the clothing or hands. Samples of venous blood are again collected at intervals of thirty minutes up to two hours. The sample at ninety minutes may be omitted. A sample of urine is collected after two hours. The blood sugar values are determined as soon as all samples are collected by any of the standard methods, e.g. Folin and Wu, or Maclean (see appendix).

Capillary blood may be used but this necessitates immediate analyses of each blood sample, which is time consuming. The sugar content of capillary and venous blood are nearly equal in the fasting state but capillary values are higher by 10 to 14 mgm. per cent. after ingestion of glucose in the normal individual, but not necessarily in the diabetic, as was shown by Cavett and Seljeskog (1933). Samples of venous blood can be transported from the wards or from outside to the laboratory without much reduction in sugar value by glycolysis over a few hours, particularly if sodium fluoride is used as an anticoagulant.

Modifications of the tolerance test have been used by several workers. Exton (1931, 1936) advocated a 2-dose dextrose test at thirty minutes interval with collection of venous blood in the fasting state and at sixty minutes. This method has given satisfactory results at the Mayo Clinic (Wilder, 1940).

Matthews *et al.* (1939) found that individuals with blood sugar values below 158 mgm. per cent. at one hour by this method were non-diabetic, whilst those with values over 180 mgm. per cent. were diabetic. A margin of doubt existed in about 7 per cent. of persons in whom the blood sugar value lay between these levels. McKean *et al.* (1935) used intravenous injection of glucose in dosage of 0.2 gm. per kgm. body weight given in ninety seconds. Blood samples were taken thereafter at three, four, five, ten and fifteen minutes. Normal persons showed blood sugar values between 150 and 175 mgm. per cent. at four minutes and below 125 mgm. per cent. at fifteen minutes. The curve in mild diabetes exceeded normal values by 50 mgm. per cent.

This method is unsuitable for routine use, since it requires injection of intravenous solutions under sterile conditions. Enocksson (1932) advocated charting the area of hyperglycæmia on squared paper and expressing this as a factor of the normal. Normal fasting blood sugar is usually found to be between 80 and 90 mgm. per cent. Values lower than this may occur.

Hart and Lisa (1940) analysed 21,000 determinations of the fasting blood sugar in non-diabetic patients and found that 11 per cent. showed values below 80 mgm. per cent., 2.3 per cent. between 60 and 70 mgm. per cent. and 1.2 per cent. below 50 mgm. per cent. Values above 100 mgm. per cent. are rarely found in the normal individual. Lyall (1946) found the fasting blood sugar to be below 100 mgm. per

cent. in a group of 268 non-diabetic glycosurics with only 11 exceptions, whilst in 41 classed as early diabetics the fasting blood sugar was above 100 mgm. per cent. in all except six. The highest value of the normal curve varies between 130 mgm. and 170 mgm. per cent. and may occasionally be lower than the former figure. Lyall found that of a group of 387 patients, the apex of the curve did not exceed 160 mgm. per cent. in 158, and was below 120 mgm. per cent. in 52. The fasting level may be reached within ninety to one hundred minutes in the healthy young adult.

In the so-called lag curve, the blood sugar rises to between 180 and 220 mgm. per cent. in thirty minutes and then returns rapidly to normal. This type of curve is rather uncommon, is rightly looked on with suspicion and cannot be reported as perfectly normal. In the pre-diabetic state, the blood sugar curve shows slight elevation above normal up to 200 mgm. per cent. and there is some delay in return to normal with values of 120 mgm. per cent. at two hours. Patients showing curves of this type should be regarded as early diabetics and treated accordingly. Even when the blood sugar value does not exceed 170 mgm. per cent., but when the values at sixty or ninety minutes exceed the thirty minutes value, it is justifiable to consider that there is delay in assimilation of glucose. In practice this is frequently accompanied by excess of urobilinogen in the urine and may indicate the earlier stages of the hepatic type of diabetes.

FACTORS WHICH INFLUENCE SUGAR TOLERANCE

When the blood sugar values rise above 220 mgm. per cent. and remain up, diabetes can be diagnosed with certainty, and generally speaking the higher the curve, the greater the severity of the diabetic state. There are exceptions to this interpretation when the patient has previously indulged in large amounts of concentrated carbohydrates or sweet drinks. The diabetic state may be much less severe after a period of careful dietetic regime. Several factors may influence the interpretation of high blood sugar curves. Septic foci, including boils, cellulitis, gangrene, and acute pancreatitis, may produce severe temporary loss of tolerance for carbohydrates, resulting in a diabetic state which may be much less severe or may even disappear after the infection is combated by sulphonamides, penicillin, insulin, surgery or other methods. Streptococcal and staphylococcal cellulitis were found to have most effect on sugar tolerance by Schmidt et al. (1934).

In *the obese patient* diminution in sugar tolerance tends to progress with years of obesity (Ogilvie, 1935; Embleton, 1938). After reduction in weight by dietetic regime, recovery of sugar tolerance to a moderate degree or even to a normal level is possible, as shown by Newburgh (1942) and by Handelsman and Schultz (1944).

In *hepatic diabetes* the earlier blood sugar values and first blood sugar curve may be no true index of the diabetic state, since amelioration is possible after careful dietetic regime and reduction in weight. Newburgh and Conn (1939) found that the blood sugar curve became normal in all except one of thirty-five cases of this type after excess weight was lost. Oxidation of glucose was found to be satisfactory by respiratory quotient determinations and no ketonuria occurred. Abnormal accumulation of fat

In most cases of glycosuria discovered during medical examinations for the Services or for life insurance, or discovered in routine medical examinations following other complications, e.g. sciatica, failing eyesight, boils, it is essential to carry out a sugar tolerance test to clarify the position.

The patient receives no food after 8 o'clock on the evening before the test. Next morning the overnight sample of urine is collected, say at 7 a.m. Urine is again passed before the test; this provides a true fasting sample of urine at 9 a.m. which is useful. If this contains sugar the condition is probably diabetes mellitus, since the majority of cases of renal glycosuria pass urine which is free of sugar in the fasting state. A sample of venous blood is taken and the patient is given 50 gm. of glucose dissolved in 3 ounces (85 c.cm.) of water. Care should be taken that no sugar is spilled over the person or over the clothing or hands. Samples of venous blood are again collected at intervals of thirty minutes up to two hours. The sample at ninety minutes may be omitted. A sample of urine is collected after two hours. The blood sugar values are determined as soon as all samples are collected by any of the standard methods, e.g. Folin and Wu, or Maclean (see appendix).

Capillary blood may be used but this necessitates immediate analyses of each blood sample, which is time consuming. The sugar content of capillary and venous blood are nearly equal in the fasting state but capillary values are higher by 10 to 14 mgm. per cent. after ingestion of glucose in the normal individual, but not necessarily in the diabetic, as was shown by Cavett and Seljeskog (1933). Samples of venous blood can be transported from the wards or from outside to the laboratory without much reduction in sugar value by glycolysis over a few hours, particularly if sodium fluoride is used as an anticoagulant.

Modifications of the tolerance test have been used by several workers. Exton (1931, 1936) advocated a 2-dose dextrose test at thirty minutes interval with collection of venous blood in the fasting state and at sixty minutes. This method has given satisfactory results at the Mayo Clinic (Wilder, 1940).

Matthews et al. (1939) found that individuals with blood sugar values below 158 mgm. per cent. at one hour by this method were non-diabetic, whilst those with values over 180 mgm. per cent. were diabetic. A margin of doubt existed in about 7 per cent. of persons in whom the blood sugar value lay between these levels. McKean et al. (1935) used intravenous injection of glucose in dosage of 0.2 gm. per kgm. body weight given in ninety seconds. Blood samples were taken thereafter at three, four, five, ten and fifteen minutes. Normal persons showed blood sugar values between 150 and 175 mgm. per cent. at four minutes and below 125 mgm. per cent. at fifteen minutes. The curve in mild diabetes exceeded normal values by 50 mgm. per cent.

This method is unsuitable for routine use, since it requires injection of intravenous solutions under sterile conditions. Enocksson (1932) advocated charting the area of hyperglycæmia on squared paper and expressing this as a factor of the normal. Normal fasting blood sugar is usually found to be between 80 and 90 mgm. per cent. Values lower than this may occur.

Hart and Lisa (1940) analysed 21,000 determinations of the fasting blood sugar in non-diabetic patients and found that 11 per cent. showed values below 80 mgm. per cent., 2.3 per cent. between 60 and 70 mgm. per cent. and 1.2 per cent. below 50 mgm. per cent. Values above 100 mgm. per cent. are rarely found in the normal individual. Lyall (1946) found the fasting blood sugar to be below 100 mgm. per

cent. in a group of 268 non-diabetic glycosurics with only 11 exceptions, whilst in 41 classed as early diabetics the fasting blood sugar was above 100 mgm. per cent. in all except six. The highest value of the normal curve varies between 130 mgm. and 170 mgm. per cent. and may occasionally be lower than the former figure. Lyall found that of a group of 387 patients, the apex of the curve did not exceed 160 mgm. per cent. in 158, and was below 120 mgm. per cent. in 52. The fasting level may be reached within ninety to one hundred minutes in the healthy young adult.

In the so-called lag curve, the blood sugar rises to between 180 and 220 mgm. per cent. in thirty minutes and then returns rapidly to normal. This type of curve is rather uncommon, is rightly looked on with suspicion and cannot be reported as perfectly normal. In the pre-diabetic state, the blood sugar curve shows slight elevation above normal up to 200 mgm. per cent. and there is some delay in return to normal with values of 120 mgm. per cent. at two hours. Patients showing curves of this type should be regarded as early diabetics and treated accordingly. Even when the blood sugar value does not exceed 170 mgm. per cent., but when the values at sixty or ninety minutes exceed the thirty minutes value, it is justifiable to consider that there is delay in assimilation of glucose.   In practice this is frequently accompanied by excess of urobilinogen in the urine and may indicate the earlier stages of the hepatic type of diabetes.

FACTORS WHICH INFLUENCE SUGAR TOLERANCE

When the blood sugar values rise above 220 mgm. per cent. and remain up, diabetes can be diagnosed with certainty, and generally speaking the higher the curve, the greater the severity of the diabetic state. There are exceptions to this interpretation when the patient has previously indulged in large amounts of concentrated carbohydrates or sweet drinks. The diabetic state may be much less severe after a period of careful dietetic regime. Several factors may influence the interpretation of high blood sugar curves. Septic foci, including boils, cellulitis, gangrene, and acute pancreatitis, may produce severe temporary loss of tolerance for carbohydrates, resulting in a diabetic state which may be much less severe or may even disappear after the infection is combated by sulphonamides, penicillin, insulin, surgery or other methods. Streptococcal and staphylococcal cellulitis were found to have most effect on sugar tolerance by Schmidt *et al.* (1934).

In *the obese patient* diminution in sugar tolerance tends to progress with years of obesity (Ogilvie, 1935; Embleton, 1938). After reduction in weight by dietetic regime, recovery of sugar tolerance to a moderate degree or even to a normal level is possible, as shown by Newburgh (1942) and by Handelsman and Schultz (1944).

In *hepatic diabetes* the earlier blood sugar values and first blood sugar curve may be no true index of the diabetic state, since amelioration is possible after careful dietetic regime and reduction in weight. Newburgh and Conn (1939) found that the blood sugar curve became normal in all except one of thirty-five cases of this type after excess weight was lost. Oxidation of glucose was found to be satisfactory by respiratory quotient determinations and no ketonuria occurred. Abnormal accumulation of fat

In most cases of glycosuria discovered during medical examinations for the Services or for life insurance, or discovered in routine medical examinations following other complications, e.g. sciatica, failing eyesight, boils, it is essential to carry out a sugar tolerance test to clarify the position.

The patient receives no food after 8 o'clock on the evening before the test. Next morning the overnight sample of urine is collected, say at 7 a.m. Urine is again passed before the test; this provides a true fasting sample of urine at 9 a.m. which is useful. If this contains sugar the condition is probably diabetes mellitus, since the majority of cases of renal glycosuria pass urine which is free of sugar in the fasting state. A sample of venous blood is taken and the patient is given 50 gm. of glucose dissolved in 3 ounces (85 c.cm.) of water. Care should be taken that no sugar is spilled over the person or over the clothing or hands. Samples of venous blood are again collected at intervals of thirty minutes up to two hours. The sample at ninety minutes may be omitted. A sample of urine is collected after two hours. The blood sugar values are determined as soon as all samples are collected by any of the standard methods, e.g. Folin and Wu, or Maclean (see appendix).

Capillary blood may be used but this necessitates immediate analyses of each blood sample, which is time consuming. The sugar content of capillary and venous blood are nearly equal in the fasting state but capillary values are higher by 10 to 14 mgm. per cent. after ingestion of glucose in the normal individual, but not necessarily in the diabetic, as was shown by Cavett and Seljeskog (1933). Samples of venous blood can be transported from the wards or from outside to the laboratory without much reduction in sugar value by glycolysis over a few hours, particularly if sodium fluoride is used as an anticoagulant.

Modifications of the tolerance test have been used by several workers. Exton (1931, 1936) advocated a 2-dose dextrose test at thirty minutes interval with collection of venous blood in the fasting state and at sixty minutes. This method has given satisfactory results at the Mayo Clinic (Wilder, 1940).

Matthews et al. (1939) found that individuals with blood sugar values below 158 mgm. per cent. at one hour by this method were non-diabetic, whilst those with values over 180 mgm. per cent. were diabetic. A margin of doubt existed in about 7 per cent. of persons in whom the blood sugar value lay between these levels. McKean et al. (1935) used intravenous injection of glucose in dosage of 0.2 gm. per kgm. body weight given in ninety seconds. Blood samples were taken thereafter at three, four, five, ten and fifteen minutes. Normal persons showed blood sugar values between 150 and 175 mgm. per cent. at four minutes and below 125 mgm. per cent. at fifteen minutes. The curve in mild diabetes exceeded normal values by 50 mgm. per cent.

This method is unsuitable for routine use, since it requires injection of intravenous solutions under sterile conditions. Enocksson (1932) advocated charting the area of hyperglycæmia on squared paper and expressing this as a factor of the normal. Normal fasting blood sugar is usually found to be between 80 and 90 mgm. per cent. Values lower than this may occur.

Hart and Lisa (1940) analysed 21,000 determinations of the fasting blood sugar in non-diabetic patients and found that 11 per cent. showed values below 80 mgm. per cent., 2.3 per cent. between 60 and 70 mgm. per cent. and 1.2 per cent. below 50 mgm. per cent. Values above 100 mgm. per cent. are rarely found in the normal individual. Lyall (1946) found the fasting blood sugar to be below 100 mgm. per

cent. in a group of 268 non-diabetic glycosurics with only 11 exceptions, whilst in 41 classed as early diabetics the fasting blood sugar was above 100 mgm. per cent. in all except six. The highest value of the normal curve varies between 130 mgm. and 170 mgm. per cent. and may occasionally be lower than the former figure. Lyall found that of a group of 387 patients, the apex of the curve did not exceed 160 mgm. per cent. in 158, and was below 120 mgm. per cent. in 52. The fasting level may be reached within ninety to one hundred minutes in the healthy young adult.

In the so-called lag curve, the blood sugar rises to between 180 and 220 mgm. per cent. in thirty minutes and then returns rapidly to normal. This type of curve is rather uncommon, is rightly looked on with suspicion and cannot be reported as perfectly normal. In the pre-diabetic state, the blood sugar curve shows slight elevation above normal up to 200 mgm. per cent. and there is some delay in return to normal with values of 120 mgm. per cent. at two hours. Patients showing curves of this type should be regarded as early diabetics and treated accordingly. Even when the blood sugar value does not exceed 170 mgm. per cent., but when the values at sixty or ninety minutes exceed the thirty minutes value, it is justifiable to consider that there is delay in assimilation of glucose. In practice this is frequently accompanied by excess of urobilinogen in the urine and may indicate the earlier stages of the hepatic type of diabetes.

FACTORS WHICH INFLUENCE SUGAR TOLERANCE

When the blood sugar values rise above 220 mgm. per cent. and remain up, diabetes can be diagnosed with certainty, and generally speaking the higher the curve, the greater the severity of the diabetic state. There are exceptions to this interpretation when the patient has previously indulged in large amounts of concentrated carbohydrates or sweet drinks. The diabetic state may be much less severe after a period of careful dietetic regime. Several factors may influence the interpretation of high blood sugar curves. Septic foci, including boils, cellulitis, gangrene, and acute pancreatitis, may produce severe temporary loss of tolerance for carbohydrates, resulting in a diabetic state which may be much less severe or may even disappear after the infection is combated by sulphonamides, penicillin, insulin, surgery or other methods. Streptococcal and staphylococcal cellulitis were found to have most effect on sugar tolerance by Schmidt *et al.* (1934).

In *the obese patient* diminution in sugar tolerance tends to progress with years of obesity (Ogilvie, 1935; Embleton, 1938). After reduction in weight by dietetic regime, recovery of sugar tolerance to a moderate degree or even to a normal level is possible, as shown by Newburgh (1942) and by Handelsman and Schultz (1944).

In *hepatic diabetes* the earlier blood sugar values and first blood sugar curve may be no true index of the diabetic state, since amelioration is possible after careful dietetic regime and reduction in weight. Newburgh and Conn (1939) found that the blood sugar curve became normal in all except one of thirty-five cases of this type after excess weight was lost. Oxidation of glucose was found to be satisfactory by respiratory quotient determinations and no ketonuria occurred. Abnormal accumulation of fat

In most cases of glycosuria discovered during medical examinations for the Services or for life insurance, or discovered in routine medical examinations following other complications, e.g. sciatica, failing eyesight, boils, it is essential to carry out a sugar tolerance test to clarify the position.

The patient receives no food after 8 o'clock on the evening before the test. Next morning the overnight sample of urine is collected, say at 7 a.m. Urine is again passed before the test; this provides a true fasting sample of urine at 9 a.m. which is useful. If this contains sugar the condition is probably diabetes mellitus, since the majority of cases of renal glycosuria pass urine which is free of sugar in the fasting state. A sample of venous blood is taken and the patient is given 50 gm. of glucose dissolved in 3 ounces (85 c.cm.) of water. Care should be taken that no sugar is spilled over the person or over the clothing or hands. Samples of venous blood are again collected at intervals of thirty minutes up to two hours. The sample at ninety minutes may be omitted. A sample of urine is collected after two hours. The blood sugar values are determined as soon as all samples are collected by any of the standard methods, e.g. Folin and Wu, or Maclean (see appendix).

Capillary blood may be used but this necessitates immediate analyses of each blood sample, which is time consuming. The sugar content of capillary and venous blood are nearly equal in the fasting state but capillary values are higher by 10 to 14 mgm. per cent. after ingestion of glucose in the normal individual, but not necessarily in the diabetic, as was shown by Cavett and Seljeskog (1933). Samples of venous blood can be transported from the wards or from outside to the laboratory without much reduction in sugar value by glycolysis over a few hours, particularly if sodium fluoride is used as an anticoagulant.

Modifications of the tolerance test have been used by several workers. Exton (1931, 1936) advocated a 2-dose dextrose test at thirty minutes interval with collection of venous blood in the fasting state and at sixty minutes. This method has given satisfactory results at the Mayo Clinic (Wilder, 1940).

Matthews et al. (1939) found that individuals with blood sugar values below 158 mgm. per cent. at one hour by this method were non-diabetic, whilst those with values over 180 mgm. per cent. were diabetic. A margin of doubt existed in about 7 per cent. of persons in whom the blood sugar value lay between these levels. McKean et al. (1935) used intravenous injection of glucose in dosage of 0.2 gm. per kgm. body weight given in ninety seconds. Blood samples were taken thereafter at three, four, five, ten and fifteen minutes. Normal persons showed blood sugar values between 150 and 175 mgm. per cent. at four minutes and below 125 mgm. per cent. at fifteen minutes. The curve in mild diabetes exceeded normal values by 50 mgm. per cent.

This method is unsuitable for routine use, since it requires injection of intravenous solutions under sterile conditions. Enocksson (1932) advocated charting the area of hyperglycæmia on squared paper and expressing this as a factor of the normal. Normal fasting blood sugar is usually found to be between 80 and 90 mgm. per cent. Values lower than this may occur.

Hart and Lisa (1940) analysed 21,000 determinations of the fasting blood sugar in non-diabetic patients and found that 11 per cent. showed values below 80 mgm. per cent., 2.3 per cent. between 60 and 70 mgm. per cent. and 1.2 per cent. below 50 mgm. per cent. Values above 100 mgm. per cent. are rarely found in the normal individual. Lyall (1946) found the fasting blood sugar to be below 100 mgm. per

RENAL GLYCOSURIA

Renal glycosuria is one of the most common conditions which require to be differentiated from diabetes mellitus. The diagnosis is determined only by a full sugar tolerance test. The relative incidence of renal glycosuria to diabetes and the pre-diabetic state in the general population is seen from figures collected in the examination of recruits for military service. Peel and Peel (1941) found 43 cases of diabetes, 9 border-line diabetics and 59 cases of renal glycosuria amongst 115 recruits showing sugar in the urine. Blotner and Hyde (1943) discovered 208 cases of diabetes, 162 cases of transient glycosuria, and 33 cases of renal glycosuria amongst 45,650 recruits. Lyall (1946) investigated 387 glycosurics amongst 40,000 recruits, of whom 41 were classified as diabetic, 111 were doubtfully diabetic, 158 were cases of renal glycosuria with blood sugar curves rising to 150 mgm. per cent., 52 were renal glycosurics with blood sugar curves rising to 120 mgm. per cent., and 21 showed persistent renal glycosuria with low values of the blood sugar.

All the evidence after twenty years of blood sugar records tends to show that renal glycosuria has no etiological association with true diabetes and very few instances are on record in which diabetes supervened in such a case, although this may be possible on the chance incidence of diabetes. In this connexion Dewes and Langner (1942) made follow-up studies in 37 of 109 persons in whom non-diabetic glycosuria had been found five to thirteen years previously. In four instances abnormal glucose curves had developed but all of these had originally higher curves than are usually accepted as normal. Vatcher and Douglas (1935) performed repeated sugar tolerance tests over periods up to seven years on 51 pensioners with symptomless glycosuria and found no evidence that diabetes followed renal glycosuria. Marble *et al.* (1939) reviewed 2,065 patients originally known to have glycosuria but not true diabetes and found that whereas 40 of a group of 240 cases of potential diabetes had in fact progressed to diabetes, none of a group of 40 cases of renal glycosuria had developed diabetes. The minor group of persistent glycosurics observed by Lyall (1946) may be confused at first sight with true diabetes, since the amount of sugar passed in the urine may amount to 3 per cent. and ketonuria may be present. Symptoms such as polyuria, abdominal discomfort and hypoglycæmic manifestations may occur. The flat blood curve alone differentiates the condition from true diabetes.

DIABETES MELLITUS IN INFANCY

The diagnosis of diabetes in childhood may be more difficult than in the adult, since blood samples may not be easily available. Capillary blood taken by finger prick or heel stab may be utilized. If a sugar tolerance test is carried out, 25 gm. of glucose is usually an adequate dose. Caution should be exercised in making a positive diagnosis of diabetes when primary ketosis has been treated with glucose. The onset of diabetes is rare before the age of seven or eight years, although I have seen the onset at the age of eighteen

in the hepatic parenchyma was suggested as the cause of limited capacity to store liver glycogen. Taub *et al.* (1945) emphasized the importance of hepatic insufficiency in mild diabetes in obese persons in the later decades and suggested that treatment should be directed to this aspect. The recognition of increased amounts of urobilinogen in the urine is a useful index of this type of diabetes accompanied by hepatic insufficiency.

The character and nature of the previous amount of *food and exercise* may influence the blood sugar curve, but only slightly under normal conditions. Starvation resulting in ketosis is followed by high values of the blood sugar if sugar is ingested. High fat diets result in high blood sugar curves, as shown by Andrews and Muether (1941), and prolonged inactivity in bed resulted in curves reaching 250 mgm. per cent., as shown by Blotner (1945), with return to normal on resumed activity.

Excessive ingestion of concentrated carbohydrates may precipitate a temporary diabetic state, as in the following instance in my records :—

A business man in the sixth decade had typical lobar pneumonia from which he made a good recovery. No sugar was present in the urine at this time. During convalescence he indulged freely in sugars, sweets and honey and complained three months later of thirst and balanitis. The blood sugar was 394 mgm. per cent. and the urine contained a large amount of sugar. A diet of 1,600 calories with 16 units protamine zinc insulin was given for one week, when the blood sugar returned to 125 mgm. per cent. Insulin was stopped and the diet increased to 2,000 and later to 2,400 calories. Later tests over six months showed normal blood sugar values, and a sugar tolerance test twelve months later gave a normal curve of the following order—72, 129, 137, 109 mgm. per cent.

Abnormal degrees of *nutritional deficiencies*, such as occur in psychopathic patients, have been shown by Robinson *et al.* (1941) to result in high blood sugar curves which may return to normal after adequate nutrition.

Previous *excessive ingestion of thyroid extract* will occasionally result in hyperglycæmia and glycosuria. The effect usually ceases within fourteen days after withdrawal of thyroid, but excessive dosage with thyroid extract may precipitate diabetes mellitus when an inherent tendency exists.

In a number of the *endocrine dyscrasias* the blood sugar curve is high. In most of these, including hyperpituitarism, and in hæmochromatosis, the diabetic state is permanent. Diabetes mellitus may coexist with thyrotoxicosis but much more frequently a raised blood sugar curve is present only during the acute thyrotoxic state. After thyroidectomy normal sugar tolerance may be established and thiouracil treatment alone may result in return to normal of the carbohydrate tolerance in thyrotoxicosis.

In a female patient aged forty years with thyrotoxicosis, glycosuria and B.M.R. plus 33 per cent., the sugar tolerance test before treatment was 133, 177, 181, 277 mgm. per cent. After treatment with thiouracil, when the patient had gained in weight, the tolerance test showed, 104, 152, 162, 141 mgm. per cent.

Severe injuries may result in temporary hyperglycæmia, especially head injuries. Thomsen (1938) found hyperglycæmia in 13.6 per cent. of patients admitted to surgical wards with trauma, and blood sugar values reaching 297, 227, and 184 mgm. per cent. in some cases. Hyperglycæmia was usually transitory.

RENAL GLYCOSURIA

Renal glycosuria is one of the most common conditions which require to be differentiated from diabetes mellitus. The diagnosis is determined only by a full sugar tolerance test. The relative incidence of renal glycosuria to diabetes and the pre-diabetic state in the general population is seen from figures collected in the examination of recruits for military service. Peel and Peel (1941) found 43 cases of diabetes, 9 border-line diabetics and 59 cases of renal glycosuria amongst 115 recruits showing sugar in the urine. Blotner and Hyde (1943) discovered 208 cases of diabetes, 162 cases of transient glycosuria, and 33 cases of renal glycosuria amongst 45,650 recruits. Lyall (1946) investigated 387 glycosurics amongst 40,000 recruits, of whom 41 were classified as diabetic, 111 were doubtfully diabetic, 158 were cases of renal glycosuria with blood sugar curves rising to 150 mgm. per cent., 52 were renal glycosurics with blood sugar curves rising to 120 mgm. per cent., and 21 showed persistent renal glycosuria with low values of the blood sugar.

All the evidence after twenty years of blood sugar records tends to show that renal glycosuria has no etiological association with true diabetes and very few instances are on record in which diabetes supervened in such a case, although this may be possible on the chance incidence of diabetes. In this connexion Dewes and Langner (1942) made follow-up studies in 37 of 109 persons in whom non-diabetic glycosuria had been found five to thirteen years previously. In four instances abnormal glucose curves had developed but all of these had originally higher curves than are usually accepted as normal. Vatcher and Douglas (1935) performed repeated sugar tolerance tests over periods up to seven years on 51 pensioners with symptomless glycosuria and found no evidence that diabetes followed renal glycosuria. Marble *et al.* (1939) reviewed 2,065 patients originally known to have glycosuria but not true diabetes and found that whereas 40 of a group of 240 cases of potential diabetes had in fact progressed to diabetes, none of a group of 40 cases of renal glycosuria had developed diabetes. The minor group of persistent glycosurics observed by Lyall (1946) may be confused at first sight with true diabetes, since the amount of sugar passed in the urine may amount to 3 per cent. and ketonuria may be present. Symptoms such as polyuria, abdominal discomfort and hypoglycæmic manifestations may occur. The flat blood curve alone differentiates the condition from true diabetes.

DIABETES MELLITUS IN INFANCY

The diagnosis of diabetes in childhood may be more difficult than in the adult, since blood samples may not be easily available. Capillary blood taken by finger prick or heel stab may be utilized. If a sugar tolerance test is carried out, 25 gm. of glucose is usually an adequate dose. Caution should be exercised in making a positive diagnosis of diabetes when primary ketosis has been treated with glucose. The onset of diabetes is rare before the age of seven or eight years, although I have seen the onset at the age of eighteen

months. As shown by White and Joslin (1933), 80 per cent. of cases of glycosuria in infancy are found to be diabetic.

DIABETIC COMA

The laboratory diagnosis of diabetic coma is usually confirmatory of the clinical findings in the uncomplicated case with hyperpnœa, acetone in the breath, a semi-comatose state, dehydration and intense glycosuria and ketonuria. The blood sugar is usually in the region of 500 mgm. per cent. but may be much higher, up to 1,850 mgm. per cent., the blood urea i moderately raised, 90 mgm. but may be over 150 mgm. per cent., th plasma CO_2 is reduced to 20 volumes per cent. and plasma chloride may b reduced. High values of the blood urea are usually of bad prognosis (Lyal and Anderson, 1932). In the typical case the blood lipids are increased and cholesterol may be raised to 400 mgm. per cent. Successful treatment with insulin and fluids results in return to normal levels of the blood chemistry within thirty hours. In known diabetic patients coma may supervene from other causes, including hypoglycæmia, cerebral hæmorrhage, coronary thrombosis, tuberculous meningitis, drug intoxications and renal failure. Here the chemical data along with the clinical manifestations are of the utmost importance in diagnosis and possible treatment. In renal failure the blood sugar may be high without sugar being present in the urine. Along with this there is evidence of gross nitrogen retention.

ILLUSTRATIVE BLOOD SUGAR CURVES

Time : minutes	Mgm. per cent.					Gm. per cent.	
	Fasting	30	6c	90	120	Urine	
						Sugar	Acetone
Normal	95	160	130	110	85	nil	nil
Renal glycosuria	85	143	120	100	80	1·0	nil
Renal diabetes	60	110	100	90	70	2·0	trace
Delayed assimilation	100	170	162	140	122	trace	nil
Pre-diabetic state	110	190	177	160	140	trace	nil
Early diabetes mellitus	120	240	180	160	140	2·0	nil
Thyrotoxicosis	80	220	150	120	90	1·0	nil
Hepatic diabetes	150	220	230	160	154	2·0	nil
Diabetes mellitus	182	284	320	280	260	3·0	+
Severe diabetes mellitus	320	440	420	382	380	4·0	+ +

In diabetic patients with acute infective states, including otitis media, abscess, carbuncle, infected gangrene and the acute abdomen, the degree of diabetic disturbance is estimated from the chemical data and the necessary steps taken for correction before operation, if such is indicated.

More difficulty is met when symptoms of the acute abdomen, severe acidosis and glycosuria coexist in a patient not previously known to have diabetes. The blood sugar and plasma CO_2 should be determined immediately. If these indicate a severe diabetic state this condition should be actively treated for twelve hours before operation, if possible.

The time factor in the diagnosis of diabetes is important. In certain instances the sugar tolerance test can be carried out at leisure, particularly if there is no evidence of ketosis. If urgency exists, no time should be lost in making the diagnosis certain. Time may be taken later to consider factors of less urgency, such as the nature of the previous diet, the existence of endocrine dyscrasias or sepsis. A series of curves is given in the accompanying table (p. 436) to assist in classification.

References

Andrews, K. R., and Muether, R. O. (1941): *J. lab. clin. Med.*, **75**, 39.
Blotner, H. (1945): *Arch. int. Med.*, **75**, 39.
——, and Hyde, R. W. (1943): *J. Amer. med. Ass.*, **122**, 432.
Cavett, J. W., and Seljeskog, S. R. (1933): *J. lab. clin. Med.*, **18**, 1103.
Dewes, E. J., and Langner, P. H., Jun. (1942): *Amer. J. med. Sci.*, **204**, 491.
Embleton, D. (1938): *Brit. med. J.*, ii, 739.
Enocksson, B. (1932): *Acta med. Scand.*, suppl. 45.
Exton, W. G. (1936): *N. Y. S. J. Med.*, **36**, 1545.
——, and Rose, A. R. (1931): *Proc. Amer. Life Insur. M. Der. Amer.*, **18**, 252.
Finley, F. G., and Rabinowitch, I. M. (1923-24): *Quart. J. Med.*, **17**, 260.
Handelsman, M. B., and Schultz, D. (1944): *Amer. J. med. Sci.*, **208**, 15.
Hart, J. F., and Lisa, J. R. (1940): *Endocrinology*, **27**, 19.
Lyall, A. (1946): *Quart. J. Med.* (in press).
——, and Anderson, A. G. (1932): *Quart. J. Med.*, N.S. **1**, 353.
McKean, P. M., Myers, G. B., and Van den Heide, E. C. (1935): *Amer. J. med. Sci.*, **189**, 702.
Marble, A., Joslin, E. P., Dublin, L. I., and Marks, H. H. (1939): *Ibid.*, **197**, 533.
Matthews, M. W., Magath, T. B., and Berkson, J. (1939): *J. Amer. med. Ass.*, **113**, 1531.
Newburgh, L. H. (1942): *Ann. int. Med.*, **17**, 935.
——, and Conn, J. W. (1939): *J. Amer. med. Ass.*, **112**, 7.
Ogilvie, R. F. (1935): *Quart. J. Med.*, N.S. **4**, 345.
Peel, A. A. F., and Peel, M. W. (1941): *Glas. med. J.*, **135**, 141.
Robinson, G. W., Jun., Shelton, P., and Smith, F. V., Jun. (1941): *Arch. int. Med.*, **68**, 945.
Schmidt, E. G., Eastland, J. S., and Burns, J. H. (1934): *Ibid.*, **54**, 466.
Taub, S. J., Shilaes, W. H., and Rice, L. (1945): *Ann. int. med.*, **22**, 852.
Thomsen, V. (1938): *Acta med. Scand.*, suppl. 91.
Vatcher, S., and Douglas, M. (1935): *J. trop. Med.*, **38**, 117.
White, P., and Joslin, E. P. (1933): "Diabetes in Childhood and Adolescence," London, p. 65.
Wilder, R. M. (1940): "Clinical Diabetes and Hyperinsulinism," London, p. 23.

APPENDIX
MACLEAN'S METHOD FOR BLOOD SUGAR ESTIMATION

Principle: An aliquot part of protein-free filtrate is boiled under standard conditions with an alkaline copper solution containing iodate and iodide. The cupric salt which has not been reduced is estimated iodometrically, titrating with thiosulphate. The difference between a blank estimation and the titration figure of the blood filtrate corresponds to the sugar in the filtrate used. The sugar content is calculated with the aid of a table already compiled.

Solutions: (1) Sodium sulphate 15 per cent.
      (2) Glacial acetic acid 50 per cent.
      (3) Dialysed iron solution (B.D.H.).
      (4) Alkaline copper solution containing potassium iodate and potassium iodide.
            Potassium bicarbonate 120 gm.
            Anhydrous potassium carbonate 80 gm.

months. As shown by White and Joslin (1933), 80 per cent. of cases of glycosuria in infancy are found to be diabetic.

DIABETIC COMA

The laboratory diagnosis of diabetic coma is usually confirmatory of the clinical findings in the uncomplicated case with hyperpnœa, acetone in the breath, a semi-comatose state, dehydration and intense glycosuria and ketonuria. The blood sugar is usually in the region of 500 mgm. per cent. but may be much higher, up to 1,850 mgm. per cent., the blood urea is moderately raised, 90 mgm. but may be over 150 mgm. per cent., the plasma CO_2 is reduced to 20 volumes per cent. and plasma chloride may be reduced. High values of the blood urea are usually of bad prognosis (Lyall and Anderson, 1932). In the typical case the blood lipids are increased and cholesterol may be raised to 400 mgm. per cent. Successful treatment with insulin and fluids results in return to normal levels of the blood chemistry within thirty hours. In known diabetic patients coma may supervene from other causes, including hypoglycæmia, cerebral hæmorrhage, coronary thrombosis, tuberculous meningitis, drug intoxications and renal failure. Here the chemical data along with the clinical manifestations are of the utmost importance in diagnosis and possible treatment. In renal failure the blood sugar may be high without sugar being present in the urine. Along with this there is evidence of gross nitrogen retention.

ILLUSTRATIVE BLOOD SUGAR CURVES

Time : minutes	Mgm. per cent.					Gm. per cent.	
	Fast-ing	30	60	90	120	Urine	
						Sugar	Acetone
Normal ..　　.. 　　..	95	160	130	110	85	nil	nil
Renal glycosuria ..　　..	85	143	120	100	80	1·0	nil
Renal diabetes ..　　..	60	110	100	90	70	2·0	trace
Delayed assimilation ..　　..	100	170	162	140	122	trace	nil
Pre-diabetic state ..　　..	110	190	177	160	140	trace	nil
Early diabetes mellitus ..　　..	120	240	180	160	140	2·0	nil
Thyrotoxicosis ..　　..	80	220	150	120	90	1·0	nil
Hepatic diabetes ..　　..	150	220	230	160	154	2·0	nil
Diabetes mellitus ..　　..	182	284	320	280	260	3·0	+
Severe diabetes mellitus ..　　..	320	440	420	382	380	4·0	++

In diabetic patients with acute infective states, including otitis media, abscess, carbuncle, infected gangrene and the acute abdomen, the degree of diabetic disturbance is estimated from the chemical data and the necessary steps taken for correction before operation, if such is indicated.

More difficulty is met when symptoms of the acute abdomen, severe acidosis and glycosuria coexist in a patient not previously known to have diabetes. The blood sugar and plasma CO_2 should be determined immediately. If these indicate a severe diabetic state this condition should be actively treated for twelve hours before operation, if possible.

(6) Folin-Wu blood sugar tubes: Test tubes graduated at 25 c.cm. and with a constricted portion above a bulb at the bottom.

Procedure

(1) *Macro method.*—A Folin-Wu filtrate is prepared by adding successively to one volume of blood seven volumes of water, one volume of 10 per cent. sodium tungstate, and one volume of 2/3 normal H_2SO_4. After mixing and allowing to stand for a few minutes until the precipitate clumps, the mixture is filtered.

In three Folin-Wu tubes are placed respectively 2 c.cm. of blood filtrate, 2 c.cm. of 0.1 per cent. glucose standard, and 2 c.cm. of 0.02 per cent. glucose standard. To each tube 2 c.cm. of alkaline copper solution are added and the contents of the tubes mixed by lateral shaking. The upper surface of the liquid lies in the constricted portion of the tube, thus reducing the amount of cuprous oxide exposed to oxidation by the air. The tubes are placed in a boiling water bath for six minutes, and then cooled in cold water for one or two minutes. To each tube are added 2 c.cm. of phosphomolybdic acid solution ; the cuprous oxide dissolves at once. After one or two minutes, the contents of the tubes are diluted to the 25 c.cm. mark with water, and thoroughly mixed.

The unknown solution is compared in a colorimeter with the standard that it most nearly matches in colour. A yellow light filter (e.g. Ilford "spectrum" yellow) facilitates colour matching.

Calculation: The standard is set at 20 mm.

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{2,000}{\text{Colorimetric reading of unknown}}$$

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{4,000}{\text{Colorimetric reading of unknown}}$$

(2) *Micro method.*—2.5 c.cm. of water are placed in a conical 15 c.cm. centrifuge tube, and 0.2 c.cm. blood added, with washing from a pipette calibrated to contain 0.2 c.cm. To the tube are then added 0.25 c.cm. of 10 per cent. sodium tungstate solution and 0.25 c.cm. of 2/3 normal H_2SO_4. The tube is stoppered, its contents thoroughly mixed, and the tube then centrifuged for several minutes.

In three Folin-Wu tubes are placed respectively 2 c.cm. of supernatant fluid from the centrifuge tube, 2 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. water. To each tube 2 c.cm. of alkaline copper solution are added and the rest of the procedure carried out as in the macro method.

Calculation: The standard is set at 20 mm.

With the weak (0.005 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{1,600}{\text{Colorimetric reading of unknown}}$$

With the strong (0.01 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{3,200}{\text{Colorimetric reading of unknown}}$$

Note: The original method of Folin and Wu (1920) as described above, gives results about 20 mgm. per 100 c.cm. higher than true blood glucose values, owing to the action of non-sugar reducing substances in blood. Benedict (1931) has modified the method to give true blood sugar values by altering the composition of the alkaline copper solution. This modified method has certain disadvantages as a routine procedure, viz:—

(a) The alkaline copper solution only keeps for six to eight weeks even on storage in a refrigerator.

(b) The blue colour produced begins to fade after ten minutes, so that no more blood filtrates must be heated together than can be read in the colorimeter within ten minutes.

References
Benedict, S. R. (1931): *J. biol. Chem.*, **92**, 141.
Folin, O., and Wu, H. (1920): *Ibid.*, **41**, 367.

Copper sulphate 3.5 gm.
Potassium iodate 0.5 gm.
Potassium iodide 5 gm.
Water to 1,000 c.cm.
(5) Sulphuric acid 25 per cent.
(6) Sodium thiosulphate N/400 prepared daily from standardized N/10 solution.
(7) A weak solution of soluble starch.

Procedure: In a 100 c.cm. Erlenmeyer flask put 23.8 c.cm. 15 per cent. sodium sulphate and two drops of 50 per cent. glacial acetic acid. Add 0.2 c.cm. blood using a Maclean's blood-sugar pipette and wash the pipette with the solution in the flask to ensure total delivery. Bring to boil to coagulate the proteins and cool in running water. Then complete the precipitation of the proteins by adding 1 c.cm. of dialysed iron, mix, and filter through a Whatman's no. 41 filter paper, 9 cm., into a 25 c.cm. cylinder. A perfectly clear filtrate should be obtained. Into another clean dry 100 c.cm. Erlenmeyer flask place accurately 2 c.cm. of the alkaline copper solution. Add 20 c.cm. of the protein-free filtrate and place on a flame standardized to bring the solution to boiling point in 100 seconds. Continue boiling for six minutes, and cool. Add 2 c.cm. of 25 per cent. sulphuric acid. When effervescence has ceased the free iodine is titrated with N/400 sodium thiosulphate, adding a few drops of starch when the solution is very pale yellow as an indicator for the remaining iodine. The end point is crystal clear. A blank estimation should be carried out simultaneously.

Calculation: e.g. Reading for blank 10.8 c.cm. N/400 thiosulphate used.
Reading for blood 8.8 c.cm. N/400 thiosulphate used.
Difference 10.8 — 8.8 = 2.0
2.0 on table gives blood sugar value of 0.109 per cent. or 109 mgm. per cent.

ESTIMATION OF BLOOD SUGAR BY THE METHOD OF FOULIN AND WU

Principle: Protein-free blood filtrate is heated with an alkaline cupric tartrate solution; some of the cupric salt is reduced to cuprous oxide by the sugar in the filtrate. Phosphomolybdic acid solution is then added, and is reduced by the cuprous oxide to a lower oxidation product of a blue colour, the intensity of which is proportional to the amount of reduced copper, and therefore to the amount of sugar in the filtrate. The blue colour produced by the blood filtrate is compared in the colorimeter with that of a standard glucose solution treated similarly.

Reagents and apparatus

(1) 10 per cent. sodium tungstate solution.
(2) 2/3 normal sulphuric acid.
(3) Alkaline copper solution: Dissolve 40 gm. of anhydrous sodium carbonate in about 400 c.cm. of water, add 7.5 gm. of tartaric acid, and when this has dissolved, transfer the fluid to a litre volumetric flask. Dissolve 4.5 gm. of crystalline cupric sulphate in about 100 c.cm. of water and transfer quantitatively to the litre flask. Mix and make up to one litre. Transfer the solution to a conical flask and boil. A slight precipitate of cuprous oxide is thrown down. Cool, filter, and make up to one litre again.
(4) Phosphomolybdic acid solution: Place 35 gm. of molybdic acid (molybdenium trioxide), 5 gm. of sodium tungstate, and 20 gm. of sodium hydroxide in 300 c.cm. of water, and warm until into solution. There is usually a greyish deposit, so filter and cool. Transfer quantitatively to a 500 c.cm. volumetric flask, using minimal quantities of wash water. Add slowly 125 c.cm. of 85 per cent. phosphoric acid, cool, and make up to 500 c.cm.
(Note: If any reduction should occur in this solution on standing, as shown by the development of a blue colour, this can be removed by adding one drop of N/10 potassium permanganate solution.)
(5) Standard glucose solutions: The stock standard is a 1 per cent. glucose solution in saturated benzoic acid solution. Working standards of 0.01 per cent. and 0.02 per cent. strength are made up by diluting 1 and 2 c.cm. of working stock standard to 100 c.cm. with saturated benzoic acid solution.

(6) Folin-Wu blood sugar tubes: Test tubes graduated at 25 c.cm. and with a constricted portion above a bulb at the bottom.

Procedure

(1) *Macro method.*—A Folin-Wu filtrate is prepared by adding successively to one volume of blood seven volumes of water, one volume of 10 per cent. sodium tungstate, and one volume of 2/3 normal H_2SO_4. After mixing and allowing to stand for a few minutes until the precipitate clumps, the mixture is filtered.

In three Folin-Wu tubes are placed respectively 2 c.cm. of blood filtrate, 2 c.cm. of 0.1 per cent. glucose standard, and 2 c.cm. of 0.02 per cent. glucose standard. To each tube 2 c.cm. of alkaline copper solution are added and the contents of the tubes mixed by lateral shaking. The upper surface of the liquid lies in the constricted portion of the tube, thus reducing the amount of cuprous oxide exposed to oxidation by the air. The tubes are placed in a boiling water bath for six minutes, and then cooled in cold water for one or two minutes. To each tube are added 2 c.cm. of phosphomolybdic acid solution ; the cuprous oxide dissolves at once. After one or two minutes, the contents of the tubes are diluted to the 25 c.cm. mark with water, and thoroughly mixed.

The unknown solution is compared in a colorimeter with the standard that it most nearly matches in colour. A yellow light filter (e.g. Ilford "spectrum" yellow) facilitates colour matching.

Calculation: The standard is set at 20 mm.

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{2,000}{\text{Colorimetric reading of unknown}}$$

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{4,000}{\text{Colorimetric reading of unknown}}$$

(2) *Micro method.*—2.5 c.cm. of water are placed in a conical 15 c.cm. centrifuge tube, and 0.2 c.cm. blood added, with washing from a pipette calibrated to contain 0.2 c.cm. To the tube are then added 0.25 c.cm. of 10 per cent. sodium tungstate solution and 0.25 c.cm. of 2/3 normal H_2SO_4. The tube is stoppered, its contents thoroughly mixed, and the tube then centrifuged for several minutes.

In three Folin-Wu tubes are placed respectively 2 c.cm. of supernatant fluid from the centrifuge tube, 2 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. water. To each tube 2 c.cm. of alkaline copper solution are added and the rest of the procedure carried out as in the macro method.

Calculation: The standard is set at 20 mm.

With the weak (0.005 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{1,600}{\text{Colorimetric reading of unknown}}$$

With the strong (0.01 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{3,200}{\text{Colorimetric reading of unknown}}$$

Note: The original method of Folin and Wu (1920) as described above, gives results about 20 mgm. per 100 c.cm. higher than true blood glucose values, owing to the action of non-sugar reducing substances in blood. Benedict (1931) has modified the method to give true blood sugar values by altering the composition of the alkaline copper solution. This modified method has certain disadvantages as a routine procedure, viz:—

(a) The alkaline copper solution only keeps for six to eight weeks even on storage in a refrigerator.

(b) The blue colour produced begins to fade after ten minutes, so that no more blood filtrates must be heated together than can be read in the colorimeter within ten minutes.

References

Benedict, S. R. (1931): *J. biol. Chem.*, 92, 141.
Folin, O., and Wu, H. (1920): *Ibid.*, 41, 367.

Copper sulphate 3.5 gm.
Potassium iodate 0.5 gm.
Potassium iodide 5 gm.
Water to 1,000 c.cm.

(5) Sulphuric acid 25 per cent.
(6) Sodium thiosulphate N/400 prepared daily from standardized N/10 solution.
(7) A weak solution of soluble starch.

Procedure: In a 100 c.cm. Erlenmeyer flask put 23.8 c.cm. 15 per cent. sodium sulphate and two drops of 50 per cent. glacial acetic acid. Add 0.2 c.cm. blood using a Maclean's blood-sugar pipette and wash the pipette with the solution in the flask to ensure total delivery. Bring to boil to coagulate the proteins and cool in running water. Then complete the precipitation of the proteins by adding 1 c.cm. of dialysed iron, mix, and filter through a Whatman's no. 41 filter paper, 9 cm., into a 25 c.cm. cylinder. A perfectly clear filtrate should be obtained. Into another clean dry 100 c.cm. Erlenmeyer flask place accurately 2 c.cm. of the alkaline copper solution. Add 20 c.cm. of the protein-free filtrate and place on a flame standardized to bring the solution to boiling point in 100 seconds. Continue boiling for six minutes, and cool. Add 2 c.cm. of 25 per cent. sulphuric acid. When effervescence has ceased the free iodine is titrated with N/400 sodium thiosulphate, adding a few drops of starch when the solution is very pale yellow as an indicator for the remaining iodine. The end point is crystal clear. A blank estimation should be carried out simultaneously.

Calculation: e.g. Reading for blank 10.8 c.cm. N/400 thiosulphate used.
Reading for blood 8.8 c.cm. N/400 thiosulphate used.
Difference 10.8 — 8.8 = 2.0
2.0 on table gives blood sugar value of 0.109 per cent. or 109 mgm. per cent.

ESTIMATION OF BLOOD SUGAR BY THE METHOD OF FOULIN AND WU

Principle: Protein-free blood filtrate is heated with an alkaline cupric tartrate solution; some of the cupric salt is reduced to cuprous oxide by the sugar in the filtrate. Phosphomolybdic acid solution is then added, and is reduced by the cuprous oxide to a lower oxidation product of a blue colour, the intensity of which is proportional to the amount of reduced copper, and therefore to the amount of sugar in the filtrate. The blue colour produced by the blood filtrate is compared in the colorimeter with that of a standard glucose solution treated similarly.

Reagents and apparatus

(1) 10 per cent. sodium tungstate solution.
(2) 2/3 normal sulphuric acid.
(3) Alkaline copper solution: Dissolve 40 gm. of anhydrous sodium carbonate in about 400 c.cm. of water, add 7.5 gm. of tartaric acid, and when this has dissolved, transfer the fluid to a litre volumetric flask. Dissolve 4.5 gm. of crystalline cupric sulphate in about 100 c.cm. of water and transfer quantitatively to the litre flask. Mix and make up to one litre. Transfer the solution to a conical flask and boil. A slight precipitate of cuprous oxide is thrown down. Cool, filter, and make up to one litre again.
(4) Phosphomolybdic acid solution: Place 35 gm. of molybdic acid (molybdenium trioxide), 5 gm. of sodium tungstate, and 20 gm. of sodium hydroxide in 300 c.cm. of water, and warm until into solution. There is usually a greyish deposit, so filter and cool. Transfer quantitatively to a 500 c.cm. volumetric flask, using minimal quantities of wash water. Add slowly 125 c.cm. of 85 per cent. phosphoric acid, cool, and make up to 500 c.cm.
(Note: If any reduction should occur in this solution on standing, as shown by the development of a blue colour, this can be removed by adding one drop of N/10 potassium permanganate solution.)
(5) Standard glucose solutions: The stock standard is a 1 per cent. glucose solution in saturated benzoic acid solution. Working standards of 0.01 per cent. and 0.02 per cent. strength are made up by diluting 1 and 2 c.cm. of working stock standard to 100 c.cm. with saturated benzoic acid solution.

(6) Folin-Wu blood sugar tubes: Test tubes graduated at 25 c.cm. and with a constricted portion above a bulb at the bottom.

Procedure

(1) *Macro method.*—A Folin-Wu filtrate is prepared by adding successively to one volume of blood seven volumes of water, one volume of 10 per cent. sodium tungstate, and one volume of 2/3 normal H_2SO_4. After mixing and allowing to stand for a few minutes until the precipitate clumps, the mixture is filtered.

In three Folin-Wu tubes are placed respectively 2 c.cm. of blood filtrate, 2 c.cm. of 0.1 per cent. glucose standard, and 2 c.cm. of 0.02 per cent. glucose standard. To each tube 2 c.cm. of alkaline copper solution are added and the contents of the tubes mixed by lateral shaking. The upper surface of the liquid lies in the constricted portion of the tube, thus reducing the amount of cuprous oxide exposed to oxidation by the air. The tubes are placed in a boiling water bath for six minutes, and then cooled in cold water for one or two minutes. To each tube are added 2 c.cm. of phosphomolybdic acid solution ; the cuprous oxide dissolves at once. After one or two minutes, the contents of the tubes are diluted to the 25 c.cm. mark with water, and thoroughly mixed.

The unknown solution is compared in a colorimeter with the standard that it most nearly matches in colour. A yellow light filter (e.g. Ilford "spectrum" yellow) facilitates colour matching.

Calculation: The standard is set at 20 mm.

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{2{,}000}{\text{Colorimetric reading of unknown}}$$

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{4{,}000}{\text{Colorimetric reading of unknown}}$$

(2) *Micro method.*—2.5 c.cm. of water are placed in a conical 15 c.cm. centrifuge tube, and 0.2 c.cm. blood added, with washing from a pipette calibrated to contain 0.2 c.cm. To the tube are then added 0.25 c.cm. of 10 per cent. sodium tungstate solution and 0.25 c.cm. of 2/3 normal H_2SO_4. The tube is stoppered, its contents thoroughly mixed, and the tube then centrifuged for several minutes.

In three Folin-Wu tubes are placed respectively 2 c.cm. of supernatant fluid from the centrifuge tube, 2 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. water. To each tube 2 c.cm. of alkaline copper solution are added and the rest of the procedure carried out as in the macro method.

Calculation: The standard is set at 20 mm.

With the weak (0.005 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{1{,}600}{\text{Colorimetric reading of unknown}}$$

With the strong (0.01 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{3{,}200}{\text{Colorimetric reading of unknown}}$$

Note: The original method of Folin and Wu (1920) as described above, gives results about 20 mgm. per 100 c.cm. higher than true blood glucose values, owing to the action of non-sugar reducing substances in blood. Benedict (1931) has modified the method to give true blood sugar values by altering the composition of the alkaline copper solution. This modified method has certain disadvantages as a routine procedure, viz:—

(a) The alkaline copper solution only keeps for six to eight weeks even on storage in a refrigerator.

(b) The blue colour produced begins to fade after ten minutes, so that no more blood filtrates must be heated together than can be read in the colorimeter within ten minutes.

References

Benedict, S. R. (1931): *J. biol. Chem.*, 92, 141.
Folin, O., and Wu. H. (1920): *Ibid.*, 41, 367.

Copper sulphate 3.5 gm.
Potassium iodate 0.5 gm.
Potassium iodide 5 gm.
Water to 1,000 c.cm.
(5) Sulphuric acid 25 per cent.
(6) Sodium thiosulphate N/400 prepared daily from standardized N/10 solution.
(7) A weak solution of soluble starch.

Procedure: In a 100 c.cm. Erlenmeyer flask put 23.8 c.cm. 15 per cent. sodium sulphate and two drops of 50 per cent. glacial acetic acid. Add 0.2 c.cm. blood using a Maclean's blood-sugar pipette and wash the pipette with the solution in the flask to ensure total delivery. Bring to boil to coagulate the proteins and cool in running water. Then complete the precipitation of the proteins by adding 1 c.cm. of dialysed iron, mix, and filter through a Whatman's no. 41 filter paper, 9 cm., into a 25 c.cm. cylinder. A perfectly clear filtrate should be obtained. Into another clean dry 100 c.cm. Erlenmeyer flask place accurately 2 c.cm. of the alkaline copper solution. Add 20 c.cm. of the protein-free filtrate and place on a flame standardized to bring the solution to boiling point in 100 seconds. Continue boiling for six minutes, and cool. Add 2 c.cm. of 25 per cent. sulphuric acid. When effervescence has ceased the free iodine is titrated with N/400 sodium thiosulphate, adding a few drops of starch when the solution is very pale yellow as an indicator for the remaining iodine. The end point is crystal clear. A blank estimation should be carried out simultaneously.

Calculation: e.g. Reading for blank 10.8 c.cm. N/400 thiosulphate used.
Reading for blood 8.8 c.cm. N/400 thiosulphate used.
Difference 10.8 — 8.8 = 2.0
2.0 on table gives blood sugar value of 0.109 per cent. or 109 mgm. per cent.

ESTIMATION OF BLOOD SUGAR BY THE METHOD OF FOULIN AND WU

Principle: Protein-free blood filtrate is heated with an alkaline cupric tartrate solution; some of the cupric salt is reduced to cuprous oxide by the sugar in the filtrate. Phosphomolybdic acid solution is then added, and is reduced by the cuprous oxide to a lower oxidation product of a blue colour, the intensity of which is proportional to the amount of reduced copper, and therefore to the amount of sugar in the filtrate. The blue colour produced by the blood filtrate is compared in the colorimeter with that of a standard glucose solution treated similarly.

Reagents and apparatus
(1) 10 per cent. sodium tungstate solution.
(2) 2/3 normal sulphuric acid.
(3) Alkaline copper solution: Dissolve 40 gm. of anhydrous sodium carbonate in about 400 c.cm. of water, add 7.5 gm. of tartaric acid, and when this has dissolved, transfer the fluid to a litre volumetric flask. Dissolve 4.5 gm. of crystalline cupric sulphate in about 100 c.cm. of water and transfer quantitatively to the litre flask. Mix and make up to one litre. Transfer the solution to a conical flask and boil. A slight precipitate of cuprous oxide is thrown down. Cool, filter, and make up to one litre again.
(4) Phosphomolybdic acid solution: Place 35 gm. of molybdic acid (molybdenium trioxide), 5 gm. of sodium tungstate, and 20 gm. of sodium hydroxide in 300 c.cm. of water, and warm until into solution. There is usually a greyish deposit, so filter and cool. Transfer quantitatively to a 500 c.cm. volumetric flask, using minimal quantities of wash water. Add slowly 125 c.cm. of 85 per cent. phosphoric acid, cool, and make up to 500 c.cm.
(Note: If any reduction should occur in this solution on standing, as shown by the development of a blue colour, this can be removed by adding one drop of N/10 potassium permanganate solution.)
(5) Standard glucose solutions: The stock standard is a 1 per cent. glucose solution in saturated benzoic acid solution. Working standards of 0.01 per cent. and 0.02 per cent. strength are made up by diluting 1 and 2 c.cm. of working stock standard to 100 c.cm. with saturated benzoic acid solution.

(6) Folin-Wu blood sugar tubes: Test tubes graduated at 25 c.cm. and with a constricted portion above a bulb at the bottom.

Procedure

(1) *Macro method.*—A Folin-Wu filtrate is prepared by adding successively to one volume of blood seven volumes of water, one volume of 10 per cent. sodium tungstate, and one volume of 2/3 normal H_2SO_4. After mixing and allowing to stand for a few minutes until the precipitate clumps, the mixture is filtered.

In three Folin-Wu tubes are placed respectively 2 c.cm. of blood filtrate, 2 c.cm. of 0.1 per cent. glucose standard, and 2 c.cm. of 0.02 per cent. glucose standard. To each tube 2 c.cm. of alkaline copper solution are added and the contents of the tubes mixed by lateral shaking. The upper surface of the liquid lies in the constricted portion of the tube, thus reducing the amount of cuprous oxide exposed to oxidation by the air. The tubes are placed in a boiling water bath for six minutes, and then cooled in cold water for one or two minutes. To each tube are added 2 c.cm. of phosphomolybdic acid solution; the cuprous oxide dissolves at once. After one or two minutes, the contents of the tubes are diluted to the 25 c.cm. mark with water, and thoroughly mixed.

The unknown solution is compared in a colorimeter with the standard that it most nearly matches in colour. A yellow light filter (e.g. Ilford "spectrum" yellow) facilitates colour matching.

Calculation: The standard is set at 20 mm.

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{2,000}{\text{Colorimetric reading of unknown}}$$

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{4,000}{\text{Colorimetric reading of unknown}}$$

(2) *Micro method.*—2.5 c.cm. of water are placed in a conical 15 c.cm. centrifuge tube, and 0.2 c.cm. blood added, with washing from a pipette calibrated to contain 0.2 c.cm. To the tube are then added 0.25 c.cm. of 10 per cent. sodium tungstate solution and 0.25 c.cm. of 2/3 normal H_2SO_4. The tube is stoppered, its contents thoroughly mixed, and the tube then centrifuged for several minutes.

In three Folin-Wu tubes are placed respectively 2 c.cm. of supernatant fluid from the centrifuge tube, 2 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. water. To each tube 2 c.cm. of alkaline copper solution are added and the rest of the procedure carried out as in the macro method.

Calculation: The standard is set at 20 mm.

With the weak (0.005 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{1,600}{\text{Colorimetric reading of unknown}}$$

With the strong (0.01 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{3,200}{\text{Colorimetric reading of unknown}}$$

Note: The original method of Folin and Wu (1920) as described above, gives results about 20 mgm. per 100 c.cm. higher than true blood glucose values, owing to the action of non-sugar reducing substances in blood. Benedict (1931) has modified the method to give true blood sugar values by altering the composition of the alkaline copper solution. This modified method has certain disadvantages as a routine procedure, viz:—

(a) The alkaline copper solution only keeps for six to eight weeks even on storage in a refrigerator.

(b) The blue colour produced begins to fade after ten minutes, so that no more blood filtrates must be heated together than can be read in the colorimeter within ten minutes.

References

Benedict, S. R. (1931): *J. biol. Chem.*, 92, 141.
Folin, O., and Wu, H. (1920): *Ibid.*, 41, 367.

Copper sulphate 3.5 gm.
Potassium iodate 0.5 gm.
Potassium iodide 5 gm.
Water to 1,000 c.cm.

(5) Sulphuric acid 25 per cent.
(6) Sodium thiosulphate N/400 prepared daily from standardized N/10 solution.
(7) A weak solution of soluble starch.

Procedure: In a 100 c.cm. Erlenmeyer flask put 23.8 c.cm. 15 per cent. sodium sulphate and two drops of 50 per cent. glacial acetic acid. Add 0.2 c.cm. *blood using a Maclean's blood-sugar pipette* and wash the pipette with the solution in the flask to ensure total delivery. Bring to boil to coagulate the proteins and cool in running water. Then complete the precipitation of the proteins by adding 1 c.cm. of dialysed iron, mix, and filter through a Whatman's no. 41 filter paper, 9 cm., into a 25 c.cm. cylinder. A perfectly clear filtrate should be obtained. Into another clean dry 100 c.cm. Erlenmeyer flask place accurately 2 c.cm. of the alkaline copper solution. Add 20 c.cm. of the protein-free filtrate and place on a flame standardized to bring the solution to boiling point in 100 seconds. Continue boiling for six minutes, and cool. Add 2 c.cm. of 25 per cent. sulphuric acid. When effervescence has ceased the free iodine is titrated with N/400 sodium thiosulphate, adding a few drops of starch when the solution is very pale yellow as an indicator for the remaining iodine. The end point is crystal clear. A blank estimation should be carried out simultaneously.

Calculation: e.g. Reading for blank 10.8 c.cm. N/400 thiosulphate used.
Reading for blood 8.8 c.cm. N/400 thiosulphate used.
Difference 10.8 — 8.8 = 2.0
2.0 on table gives blood sugar value of *0.109 per cent.* or 109 mgm. per cent.

ESTIMATION OF BLOOD SUGAR BY THE METHOD OF FOULIN AND WU

Principle: Protein-free blood filtrate is heated with an alkaline cupric tartrate solution; some of the cupric salt is reduced to cuprous oxide by the sugar in the filtrate. Phosphomolybdic acid solution is then added, and is reduced by the cuprous oxide to a lower oxidation product of a blue colour, the intensity of which is proportional to the amount of reduced copper, and therefore to the amount of sugar in the filtrate. The blue colour produced by the blood filtrate is compared in the colorimeter with that of a standard glucose solution treated similarly.

Reagents and apparatus

(1) 10 per cent. sodium tungstate solution.
(2) 2/3 normal sulphuric acid.
(3) Alkaline copper solution: Dissolve 40 gm. of anhydrous sodium carbonate in about 400 c.cm. of water, add 7.5 gm. of tartaric acid, and when this has dissolved, transfer the fluid to a litre volumetric flask. Dissolve 4.5 gm. of crystalline cupric sulphate in about 100 c.cm. of water and transfer quantitatively to the litre flask. Mix and make up to one litre. Transfer the solution to a conical flask and boil. A slight precipitate of cuprous oxide is thrown down. Cool, filter, and make up to one litre again.
(4) Phosphomolybdic acid solution: Place 35 gm. of molybdic acid (molybdenium trioxide), 5 gm. of sodium tungstate, and 20 gm. of sodium hydroxide in 300 c.cm. of water, and warm until into solution. There is usually a greyish deposit, so filter and cool. Transfer quantitatively to a 500 c.cm. volumetric flask, using minimal quantities of wash water. Add slowly 125 c.cm. of 85 per cent. phosphoric acid, cool, and make up to 500 c.cm.
(Note: If any reduction should occur in this solution on standing, as shown by the development of a blue colour, this can be removed by adding one drop of N/10 potassium permanganate solution.)
(5) Standard glucose solutions: The stock standard is a 1 per cent. glucose solution in saturated benzoic acid solution. Working standards of 0.01 per cent. and 0.02 per cent. strength are made up by diluting 1 and 2 c.cm. of working stock standard to 100 c.cm. with saturated benzoic acid solution.

(6) Folin-Wu blood sugar tubes: Test tubes graduated at 25 c.cm. and with a constricted portion above a bulb at the bottom.

Procedure

(1) *Macro method.*—A Folin-Wu filtrate is prepared by adding successively to one volume of blood seven volumes of water, one volume of 10 per cent. sodium tungstate, and one volume of $2/3$ normal H_2SO_4. After mixing and allowing to stand for a few minutes until the precipitate clumps, the mixture is filtered.

In three Folin-Wu tubes are placed respectively 2 c.cm. of blood filtrate, 2 c.cm. of 0.1 per cent. glucose standard, and 2 c.cm. of 0.02 per cent. glucose standard. To each tube 2 c.cm. of alkaline copper solution are added and the contents of the tubes mixed by lateral shaking. The upper surface of the liquid lies in the constricted portion of the tube, thus reducing the amount of cuprous oxide exposed to oxidation by the air. The tubes are placed in a boiling water bath for six minutes, and then cooled in cold water for one or two minutes. To each tube are added 2 c.cm. of phosphomolybdic acid solution ; the cuprous oxide dissolves at once. After one or two minutes, the contents of the tubes are diluted to the 25 c.cm. mark with water, and thoroughly mixed.

The unknown solution is compared in a colorimeter with the standard that it most nearly matches in colour. A yellow light filter (e.g. Ilford "spectrum" yellow) facilitates colour matching.

Calculation: The standard is set at 20 mm.

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{2,000}{\text{Colorimetric reading of unknown}}$$

With the 0.01 per cent. glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{4,000}{\text{Colorimetric reading of unknown}}$$

(2) *Micro method.*—2.5 c.cm. of water are placed in a conical 15 c.cm. centrifuge tube, and 0.2 c.cm. blood added, with washing from a pipette calibrated to contain 0.2 c.cm. To the tube are then added 0.25 c.cm. of 10 per cent. sodium tungstate solution and 0.25 c.cm. of $2/3$ normal H_2SO_4. The tube is stoppered, its contents thoroughly mixed, and the tube then centrifuged for several minutes.

In three Folin-Wu tubes are placed respectively 2 c.cm. of supernatant fluid from the centrifuge tube, 2 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. of 0.01 per cent. glucose standard and 1 c.cm. water. To each tube 2 c.cm. of alkaline copper solution are added and the rest of the procedure carried out as in the macro method.

Calculation: The standard is set at 20 mm.

With the weak (0.005 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{1,600}{\text{Colorimetric reading of unknown}}$$

With the strong (0.01 per cent.) glucose standard, mgm. sugar per 100 c.cm. blood

$$= \frac{3,200}{\text{Colorimetric reading of unknown}}$$

Note: The original method of Folin and Wu (1920) as described above, gives results about 20 mgm. per 100 c.cm. higher than true blood glucose values, owing to the action of non-sugar reducing substances in blood. Benedict (1931) has modified the method to give true blood sugar values by altering the composition of the alkaline copper solution. This modified method has certain disadvantages as a routine procedure, viz:—

(a) The alkaline copper solution only keeps for six to eight weeks even on storage in a refrigerator.

(b) The blue colour produced begins to fade after ten minutes, so that no more blood filtrates must be heated together than can be read in the colorimeter within ten minutes.

References

Benedict, S. R. (1931): *J. biol. Chem.*, 92, 141.
Folin, O., and Wu, H. (1920): *Ibid.*, 41, 367.

DIABETES FROM THE PATIENT'S POINT OF VIEW

BY A DIABETIC DOCTOR

No clinician who experiences perfect health can have a first-hand knowledge of medicine. He may have an encyclopædic knowledge of the signs of disease and of the pathological changes associated with it, and he may know all that is to be known of the symptoms of disease as his patients describe them, but he still lacks the understanding of what these symptoms and signs really mean to the patient who is afflicted by them. This knowledge can only be secured by the personal experience of disease. Yet even this personal experience cannot reveal all its secrets to him, for no disease is uniform in its manifestations and he can only experience one form as it affects him personally.

I had always had a considerable interest in diabetes, but it was only when I became diabetic myself that I really began to appreciate the problems of the diabetic life. Even so, I can only speak with the experience of one particular form of this pleomorphic disease—that of acute diabetes mellitus of the insulin-sensitive type occurring in a young adult during war time.

These five years of my diabetic experience fall into five fairly well-defined periods:—

(1) PERIOD OF DIAGNOSIS AND EARLY INITIATION

I diagnosed my own diabetes and so it was to myself that I said "You have diabetes". I had said this before to patients without realizing the turmoil of fear and uncertainty, the vista of invalidism, and even the indignation that these words could arouse. I had, of course, always followed this bald statement to my patients with reassurances: "Nowadays diabetes can be treated, a full life can be led; a few inconveniences, perhaps, but no more". Of course I reassured myself, and my colleagues valiantly added their reassurances to mine, but how unconvincing and unsatisfying it all was with no backing of experience!

Within a few hours of having first seen my urine turn Benedict's solution red before it even boiled, I was in bed in the ward, on the wrong side of the fence that doctors so carefully erect and maintain between themselves and their patients. And so, with resignation, to study anew the problems of balancing diet and insulin with which I had thought myself familiar enough already to be able to instruct my diabetic patients. How simple it had then seemed, and how complicated now. In future no meal would be an elegant satisfaction of appetite, but a problem in arithmetic and a trial of self-negation. No longer would I live my life at the behest of work and leisure, but to a clockwork routine of injections and measured meals. Holidays, I read, were times of special risk. Wherever I went I should be encumbered

by the paraphernalia of urine testing, balances, weights and measuring glasses. Finally, I had the threat of carbuncles, blindness and gangrene lurking in the distance to keep me to the narrow lines of the diabetic life. These fears and threats are not the peculiar dread of the medical man. Most lay patients have, or soon hear of, some relation or friend who lives a restricted diabetic life, or who suffers from some major complication of the disease. Here, then, is a real need of the diabetic at the time of diagnosis. To be able to meet and talk at leisure to an active and competent established diabetic who can show by example how needless are the fears and worries. It is not enough to read about such people—as in Joslin's handbook, excellent as it may be—the need is to meet and talk to them. Every diabetic clinic should provide an opportunity for the new patients to be introduced to, and to get to know, one or two established diabetics who have learnt to live the diabetic life at its fullest.

(2) PERIOD OF INITIATION AND EARLY STUDY

Learning the composition of the commoner foods is not laborious if it is attempted item by item. With each meal in hospital I looked up the carbohydrate content of every new thing that I ate, and I found my dietary vocabulary extending quickly without effort. (How many diabetics are given a list of food values to consult as they eat their first measured meals in hospital?) Soon I was enjoying checking up the composition of the meals that the dietitian sent me, hoping to catch her out. At first I restricted my attention to the carbohydrate content of foods, neglecting, for simplicity, the more complicated estimates of protein and fat.

I prescribed and, of course, injected my own insulin, in consultation with my chief. This privilege was mine because of my medicial training; but why should not all diabetics be trained in hospital to do this? They should be asked to suggest what dose they should be given each time, and if wrong, be told why they were wrong. Starting on two doses of soluble insulin I was soon taking a single dose of protamine zinc insulin.

Naturally I tested my own urine, and learnt from experience that there are emotional as well as colour reactions to the tests. A blue specimen was "correct", "normal" and somehow spelt recovery: a yellow or red test seemed to signal danger and relapse. I am sure that this sort of reaction is common among diabetics and effort must be spent in dispelling it. I found it hard to overcome until, with experience, I came to associate a small amount of sugar in the urine with a feeling of security from hypoglycæmia. More attention should be given to assuring patients that the urine need only be sugar-free at those times of day when the insulin dose should be exerting its maximum action, and to vigorous reassurance as to the harmlessness of sugary tests after meals.

Hypoglycæmic reactions I learnt to recognize with ease, particularly because of my interest in their nature. All diabetics should be trained to study their reactions to hypoglycæmia, and be warned to look out for

DIABETES FROM THE PATIENT'S POINT OF VIEW

By A DIABETIC DOCTOR

No clinician who experiences perfect health can have a first-hand knowledge of medicine. He may have an encyclopædic knowledge of the signs of disease and of the pathological changes associated with it, and he may know all that is to be known of the symptoms of disease as his patients describe them, but he still lacks the understanding of what these symptoms and signs really mean to the patient who is afflicted by them. This knowledge can only be secured by the personal experience of disease. Yet even this personal experience cannot reveal all its secrets to him, for no disease is uniform in its manifestations and he can only experience one form as it affects him personally.

I had always had a considerable interest in diabetes, but it was only when I became diabetic myself that I really began to appreciate the problems of the diabetic life. Even so, I can only speak with the experience of one particular form of this pleomorphic disease—that of acute diabetes mellitus of the insulin-sensitive type occurring in a young adult during war time.

These five years of my diabetic experience fall into five fairly well-defined periods:—

(1) PERIOD OF DIAGNOSIS AND EARLY INITIATION

I diagnosed my own diabetes and so it was to myself that I said "You have diabetes". I had said this before to patients without realizing the turmoil of fear and uncertainty, the vista of invalidism, and even the indignation that these words could arouse. I had, of course, always followed this bald statement to my patients with reassurances: "Nowadays diabetes can be treated, a full life can be led; a few inconveniences, perhaps, but no more". Of course I reassured myself, and my colleagues valiantly added their reassurances to mine, but how unconvincing and unsatisfying it all was with no backing of experience!

Within a few hours of having first seen my urine turn Benedict's solution red before it even boiled, I was in bed in the ward, on the wrong side of the fence that doctors so carefully erect and maintain between themselves and their patients. And so, with resignation, to study anew the problems of balancing diet and insulin with which I had thought myself familiar enough already to be able to instruct my diabetic patients. How simple it had then seemed, and how complicated now. In future no meal would be an elegant satisfaction of appetite, but a problem in arithmetic and a trial of self-negation. No longer would I live my life at the behest of work and leisure, but to a clockwork routine of injections and measured meals. Holidays, I read, were times of special risk. Wherever I went I should be encumbered ·

by the paraphernalia of urine testing, balances, weights and measuring glasses. Finally, I had the threat of carbuncles, blindness and gangrene lurking in the distance to keep me to the narrow lines of the diabetic life. These fears and threats are not the peculiar dread of the medical man. Most lay patients have, or soon hear of, some relation or friend who lives a restricted diabetic life, or who suffers from some major complication of the disease. Here, then, is a real need of the diabetic at the time of diagnosis. To be able to meet and talk at leisure to an active and competent established diabetic who can show by example how needless are the fears and worries. It is not enough to read about such people—as in Joslin's handbook, excellent as it may be—the need is to meet and talk to them. Every diabetic clinic should provide an opportunity for the new patients to be introduced to, and to get to know, one or two established diabetics who have learnt to live the diabetic life at its fullest.

(2) PERIOD OF INITIATION AND EARLY STUDY

Learning the composition of the commoner foods is not laborious if it is attempted item by item. With each meal in hospital I looked up the carbohydrate content of every new thing that I ate, and I found my dietary vocabulary extending quickly without effort. (How many diabetics are given a list of food values to consult as they eat their first measured meals in hospital?) Soon I was enjoying checking up the composition of the meals that the dietitian sent me, hoping to catch her out. At first I restricted my attention to the carbohydrate content of foods, neglecting, for simplicity, the more complicated estimates of protein and fat.

I prescribed and, of course, injected my own insulin, in consultation with my chief. This privilege was mine because of my medicial training; but why should not all diabetics be trained in hospital to do this? They should be asked to suggest what dose they should be given each time, and if wrong, be told why they were wrong. Starting on two doses of soluble insulin I was soon taking a single dose of protamine zinc insulin.

Naturally I tested my own urine, and learnt from experience that there are emotional as well as colour reactions to the tests. A blue specimen was "correct", "normal" and somehow spelt recovery: a yellow or red test seemed to signal danger and relapse. I am sure that this sort of reaction is common among diabetics and effort must be spent in dispelling it. I found it hard to overcome until, with experience, I came to associate a small amount of sugar in the urine with a feeling of security from hypoglycæmia. More attention should be given to assuring patients that the urine need only be sugar-free at those times of day when the insulin dose should be exerting its maximum action, and to vigorous reassurance as to the harmlessness of sugary tests after meals.

Hypoglycæmic reactions I learnt to recognize with ease, particularly because of my interest in their nature. All diabetics should be trained to study their reactions to hypoglycæmia, and be warned to look out for

variations in them. No diabetic should leave hospital without considerable experience of hypoglycæmia and of its relief with the taking of sugar.

(3) PERIOD OF EARLY EXPERIENCE

Before returning to work I had a few weeks of convalescent holiday with friends. During these weeks I began to apply what I had learnt in hospital to the circumstances of everyday life. It was a period of decreasing insulin requirement, and I found the habit of frequent urine testing of great value. I kept a careful chart of the tests and of my insulin dosage.

Dietary problems were less difficult than I had expected. Soon I became accurate at guessing the weights of the chief carbohydrate foods. I had my scales always on the table, guessed at first, and then checked the guess by weighing. I still only took account of carbohydrate, and here I must express my conviction that this is all that most diabetics need do. Variations of fat and protein (especially with food rationing) are not great on a free diet, and in any case they affect the blood sugar level less immediately than carbohydrate, which must be correctly distributed throughout the day to balance insulin action. There is little difficulty in keeping account of carbohydrate during a meal, but it is not easy to carry three separate sums in one's head, and to account for protein and fat in addition may interfere with the carrying on of intelligent conversation. To lay too great a burden of calculation at meals on a diabetic may result in all attempts at a measured diet being forsaken, or in restriction to a set diet sheet with meals taken at home as the only possibility. The necessity for calculating protein and fat is one main objection to the "calorie control" method of diabetic dieting.

The chief difficulty is found with dishes containing an intimate mixture of carbohydrate, protein and fat, such as a stew, kedgeree or cottage pie. Usually the carbohydrate can be recognized and estimated, but sometimes it is necessary to ask one's host to avoid such dishes. In a restaurant they can nearly always be avoided. In order to gain experience of such dishes I found it useful to frequent the kitchen. Here I could see what are the constituents of common mixed dishes, and in particular learn the many forms under which flour is used in cooking. I have learnt many valuable lessons by watching my wife cooking, weighing all the constituents as they are used, and then weighing the final product and calculating the size of portion that contains, say, 5 gm. of carbohydrate.

My diet at first contained 200 gm. carbohydrate. Although a generous allowance by most standards, this was only half the amount to which I had been accustomed in my pre-diabetic days, and I found it required quite an effort of discipline not to exceed my ration. Later I increased my carbohydrate to 280 gm. and I was surprised to find, not only how much pleasanter the diet became, but also how much fitter I felt. For the young insulin-sensitive type of diabetic I am sure the diet should be satisfying. Such a diet will be willingly adhered to, and only leads to a small increase in insulin requirement. The only difficulty to which it may lead (especially

since bread rationing) is that a meal may be encountered away from home in which the carbohydrate provided is inadequate. Usually an extra helping of potatoes can be secured. If not, the sugar in one's pocket must be drawn upon, but these occasions are uncommon.

In these early days I learnt the tricks of painless injection: the overriding importance of a sharp needle, the existence of pain-free spots in the skin. Local reactions I found troublesome, but a change to another make of insulin and care to avoid too shallow injection eliminated them. The injections are now quite the least irksome feature of my diabetes.

At this time I also began to learn the management of hypoglycæmia. I experienced the curious prejudice that so many diabetics feel against taking sugar in hypoglycæmia. Carbohydrate is rationed, one likes to keep it all for meal times, why waste the daily ration on an unsatisfying lump of sugar? At the earliest symptoms one is in doubt; "Is this really it?" one thinks, "better wait and see". One knows that sugar taken unnecessarily may result in a sugary test and in the early days this is still distressing. How important it is to insist that on the slightest suspicion of hypoglycæmia sugar must be taken *at once*. I find that when I have "waited and seen" I have always found my suspicion was right and I am faced with a far more uncomfortable reaction than I would have had, had I taken sugar on the first suspicion. I find that vita-glucose tablets are the most convenient form of sugar. How important it is to insist that sugar must be carried everywhere! I learnt my lesson when I became hypoglycæmic at the tenth hole on a golf course, with my sugar in my jacket, back at the club house. Luckily a cottage was near, but I felt pretty foolish as I knocked at the door and asked for a crust of bread. I had a long wait before I could continue my round of golf.

The other important lesson I learnt, but slowly, was the prophylaxis of hypoglycæmia: to take extra carbohydrate before exercise, to take sugar if luncheon is late (not to wait and sweat through the first course), and especially to take sugar whenever it is necessary to drive the car before meals. Driving home after work in the evenings is a dangerous time for diabetics taking protamine zinc insulin.

(4) PERIOD OF INCREASING EXPERIENCE

Most of the lessons of the diabetic life are learnt in the first six months or year, and this is a period during which a diabetic needs much encouragement to venture out into all the normal activities of a busy life. In most cases, as in mine, it will be a period of increasing insulin requirement during which fairly frequent urine tests and a careful record of them will be most valuable in teaching the business of adjusting insulin dosage to need. One of the things I have learnt from my record is that even when I am keeping most strictly to my diet I have occasional big swings of blood sugar level from which I seem to take no harm (and there is no theoretical reason for supposing that such swings will ever be harmful). This being so I am not alarmed at brief hyperglycæmia resulting from inevitable breaches of

variations in them. No diabetic should leave hospital without considerable experience of hypoglycæmia and of its relief with the taking of sugar.

(3) PERIOD OF EARLY EXPERIENCE

Before returning to work I had a few weeks of convalescent holiday with friends. During these weeks I began to apply what I had learnt in hospital to the circumstances of everyday life. It was a period of decreasing insulin requirement, and I found the habit of frequent urine testing of great value. I kept a careful chart of the tests and of my insulin dosage.

Dietary problems were less difficult than I had expected. Soon I became accurate at guessing the weights of the chief carbohydrate foods. I had my scales always on the table, guessed at first, and then checked the guess by weighing. I still only took account of carbohydrate, and here I must express my conviction that this is all that most diabetics need do. Variations of fat and protein (especially with food rationing) are not great on a free diet, and in any case they affect the blood sugar level less immediately than carbohydrate, which must be correctly distributed throughout the day to balance insulin action. There is little difficulty in keeping account of carbohydrate during a meal, but it is not easy to carry three separate sums in one's head, and to account for protein and fat in addition may interfere with the carrying on of intelligent conversation. To lay too great a burden of calculation at meals on a diabetic may result in all attempts at a measured diet being forsaken, or in restriction to a set diet sheet with meals taken at home as the only possibility. The necessity for calculating protein and fat is one main objection to the "calorie control" method of diabetic dieting.

The chief difficulty is found with dishes containing an intimate mixture of carbohydrate, protein and fat, such as a stew, kedgeree or cottage pie. Usually the carbohydrate can be recognized and estimated, but sometimes it is necessary to ask one's host to avoid such dishes. In a restaurant they can nearly always be avoided. In order to gain experience of such dishes I found it useful to frequent the kitchen. Here I could see what are the constituents of common mixed dishes, and in particular learn the many forms under which flour is used in cooking. I have learnt many valuable lessons by watching my wife cooking, weighing all the constituents as they are used, and then weighing the final product and calculating the size of portion that contains, say, 5 gm. of carbohydrate.

My diet at first contained 200 gm. carbohydrate. Although a generous allowance by most standards, this was only half the amount to which I had been accustomed in my pre-diabetic days, and I found it required quite an effort of discipline not to exceed my ration. Later I increased my carbohydrate to 280 gm. and I was surprised to find, not only how much pleasanter the diet became, but also how much fitter I felt. For the young insulin-sensitive type of diabetic I am sure the diet should be satisfying. Such a diet will be willingly adhered to, and only leads to a small increase in insulin requirement. The only difficulty to which it may lead (especially

since bread rationing) is that a meal may be encountered away from home in which the carbohydrate provided is inadequate. Usually an extra helping of potatoes can be secured. If not, the sugar in one's pocket must be drawn upon, but these occasions are uncommon.

In these early days I learnt the tricks of painless injection: the overriding importance of a sharp needle, the existence of pain-free spots in the skin. Local reactions I found troublesome, but a change to another make of insulin and care to avoid too shallow injection eliminated them. The injections are now quite the least irksome feature of my diabetes.

At this time I also began to learn the management of hypoglycæmia. I experienced the curious prejudice that so many diabetics feel against taking sugar in hypoglycæmia. Carbohydrate is rationed, one likes to keep it all for meal times, why waste the daily ration on an unsatisfying lump of sugar? At the earliest symptoms one is in doubt; "Is this really it?" one thinks, "better wait and see". One knows that sugar taken unnecessarily may result in a sugary test and in the early days this is still distressing. How important it is to insist that on the slightest suspicion of hypoglycæmia sugar must be taken *at once*. I find that when I have "waited and seen" I have always found my suspicion was right and I am faced with a far more uncomfortable reaction than I would have had, had I taken sugar on the first suspicion. I find that vita-glucose tablets are the most convenient form of sugar. How important it is to insist that sugar must be carried everywhere! I learnt my lesson when I became hypoglycæmic at the tenth hole on a golf course, with my sugar in my jacket, back at the club house. Luckily a cottage was near, but I felt pretty foolish as I knocked at the door and asked for a crust of bread. I had a long wait before I could continue my round of golf.

The other important lesson I learnt, but slowly, was the prophylaxis of hypoglycæmia: to take extra carbohydrate before exercise, to take sugar if luncheon is late (not to wait and sweat through the first course), and especially to take sugar whenever it is necessary to drive the car before meals. Driving home after work in the evenings is a dangerous time for diabetics taking protamine zinc insulin.

(4) PERIOD OF INCREASING EXPERIENCE

Most of the lessons of the diabetic life are learnt in the first six months or year, and this is a period during which a diabetic needs much encouragement to venture out into all the normal activities of a busy life. In most cases, as in mine, it will be a period of increasing insulin requirement during which fairly frequent urine tests and a careful record of them will be most valuable in teaching the business of adjusting insulin dosage to need. One of the things I have learnt from my record is that even when I am keeping most strictly to my diet I have occasional big swings of blood sugar level from which I seem to take no harm (and there is no theoretical reason for supposing that such swings will ever be harmful). This being so I am not alarmed at brief hyperglycæmia resulting from inevitable breaches of

variations in them. No diabetic should leave hospital without considerable experience of hypoglycæmia and of its relief with the taking of sugar.

(3) PERIOD OF EARLY EXPERIENCE

Before returning to work I had a few weeks of convalescent holiday with friends. During these weeks I began to apply what I had learnt in hospital to the circumstances of everyday life. It was a period of decreasing insulin requirement, and I found the habit of frequent urine testing of great value. I kept a careful chart of the tests and of my insulin dosage.

Dietary problems were less difficult than I had expected. Soon I became accurate at guessing the weights of the chief carbohydrate foods. I had my scales always on the table, guessed at first, and then checked the guess by weighing. I still only took account of carbohydrate, and here I must express my conviction that this is all that most diabetics need do. Variations of fat and protein (especially with food rationing) are not great on a free diet, and in any case they affect the blood sugar level less immediately than carbohydrate, which must be correctly distributed throughout the day to balance insulin action. There is little difficulty in keeping account of carbohydrate during a meal, but it is not easy to carry three separate sums in one's head, and to account for protein and fat in addition may interfere with the carrying on of intelligent conversation. To lay too great a burden of calculation at meals on a diabetic may result in all attempts at a measured diet being forsaken, or in restriction to a set diet sheet with meals taken at home as the only possibility. The necessity for calculating protein and fat is one main objection to the "calorie control" method of diabetic dieting.

The chief difficulty is found with dishes containing an intimate mixture of carbohydrate, protein and fat, such as a stew, kedgeree or cottage pie. Usually the carbohydrate can be recognized and estimated, but sometimes it is necessary to ask one's host to avoid such dishes. In a restaurant they can nearly always be avoided. In order to gain experience of such dishes I found it useful to frequent the kitchen. Here I could see what are the constituents of common mixed dishes, and in particular learn the many forms under which flour is used in cooking. I have learnt many valuable lessons by watching my wife cooking, weighing all the constituents as they are used, and then weighing the final product and calculating the size of portion that contains, say, 5 gm. of carbohydrate.

My diet at first contained 200 gm. carbohydrate. Although a generous allowance by most standards, this was only half the amount to which I had been accustomed in my pre-diabetic days, and I found it required quite an effort of discipline not to exceed my ration. Later I increased my carbohydrate to 280 gm. and I was surprised to find, not only how much pleasanter the diet became, but also how much fitter I felt. For the young insulin-sensitive type of diabetic I am sure the diet should be satisfying. Such a diet will be willingly adhered to, and only leads to a small increase in insulin requirement. The only difficulty to which it may lead (especially

since bread rationing) is that a meal may be encountered away from home in which the carbohydrate provided is inadequate. Usually an extra helping of potatoes can be secured. If not, the sugar in one's pocket must be drawn upon, but these occasions are uncommon.

In these early days I learnt the tricks of painless injection: the overriding importance of a sharp needle, the existence of pain-free spots in the skin. Local reactions I found troublesome, but a change to another make of insulin and care to avoid too shallow injection eliminated them. The injections are now quite the least irksome feature of my diabetes.

At this time I also began to learn the management of hypoglycæmia. I experienced the curious prejudice that so many diabetics feel against taking sugar in hypoglycæmia. Carbohydrate is rationed, one likes to keep it all for meal times, why waste the daily ration on an unsatisfying lump of sugar? At the earliest symptoms one is in doubt; "Is this really it?" one thinks, "better wait and see". One knows that sugar taken unnecessarily may result in a sugary test and in the early days this is still distressing. How important it is to insist that on the slightest suspicion of hypoglycæmia sugar must be taken *at once*. I find that when I have "waited and seen" I have always found my suspicion was right and I am faced with a far more uncomfortable reaction than I would have had, had I taken sugar on the first suspicion. I find that vita-glucose tablets are the most convenient form of sugar. How important it is to insist that sugar must be carried everywhere! I learnt my lesson when I became hypoglycæmic at the tenth hole on a golf course, with my sugar in my jacket, back at the club house. Luckily a cottage was near, but I felt pretty foolish as I knocked at the door and asked for a crust of bread. I had a long wait before I could continue my round of golf.

The other important lesson I learnt, but slowly, was the prophylaxis of hypoglycæmia: to take extra carbohydrate before exercise, to take sugar if luncheon is late (not to wait and sweat through the first course), and especially to take sugar whenever it is necessary to drive the car before meals. Driving home after work in the evenings is a dangerous time for diabetics taking protamine zinc insulin.

(4) PERIOD OF INCREASING EXPERIENCE

Most of the lessons of the diabetic life are learnt in the first six months or year, and this is a period during which a diabetic needs much encouragement to venture out into all the normal activities of a busy life. In most cases, as in mine, it will be a period of increasing insulin requirement during which fairly frequent urine tests and a careful record of them will be most valuable in teaching the business of adjusting insulin dosage to need. One of the things I have learnt from my record is that even when I am keeping most strictly to my diet I have occasional big swings of blood sugar level from which I seem to take no harm (and there is no theoretical reason for supposing that such swings will ever be harmful). This being so I am not alarmed at brief hyperglycæmia resulting from inevitable breaches of

diet. A diabetic who is living a normal social life must meet occasions when it is impossible to estimate carbohydrate accurately. It is therefore necessary to err on the generous side and be undismayed if heavy glycosuria results.

Perhaps the most important lesson I learnt during this period was that hypoglycæmic symptoms are constantly changing. At first my symptoms were those due to adrenaline action—sweating, tremor and palpitation— quite characteristic and easy to recognize. After a few months, these gave way to ocular symptoms—dimness of vision and occasional diplopia. Emotional symptoms finally became more prominent—irritability or hilarity. These are more easily recognized by my wife than by myself (I have learnt the wisdom of taking sugar on her advice, even when I see no need myself). The symptoms are occasionally very indefinite; just a vague feeling of uneasiness for which I have to keep a careful watch at the times of maximum insulin action.

I took a mixture of protamine zinc and soluble insulin at first, but after a time I found it inconvenient and have changed to two doses of ordinary insulin. The reason is that a dose of P.Z.I. demands that tea and supper should be taken at the correct time. It is no pleasure (as was once my lot) to eat sugar throughout a performance at the theatre and to be unable to join the rest of the party at supper afterwards. Breakfast and lunch are fixtures in nearly everyone's life and can cover the morning dose of soluble insulin. Tea can be dispensed with and supper is a movable feast and can be much more easily covered by an evening dose taken just before the meal. I make it a rule to take the evening dose immediately before supper. It is unwise, when going out to supper, to take the dose at home before starting: I have once done this and been in difficulties when the lateness of a fellow guest delayed the meal for an hour. Moreover, there is always the risk of delay, or even an accident, on the journey to a meal away from home. There is never any difficulty in asking to "wash one's hands" before the meal in order to give the injection.

During this period a diabetic will probably experience his first attack of a cold or "flu", which will almost certainly demand a large increase of insulin requirement. It was during my first experience of a bout of influenza after I became diabetic that I fully realized the advantage of my medical training, in that I was not afraid to increase my insulin boldly. How little teaching would be necessary to enable any intelligent diabetic to do this! Frequent urine testing is, of course, the secret. I adopt four-hourly testing. I take my normal dose of insulin and then give myself an extra six units of insulin after each "red" test, and keep glucose handy in case of any suspicion of hypoglycæmia. On the second day I add on to the morning dose the total number of extra units that I had to take on the first day and on to the evening the extra units I required the previous evening. In this way it is possible to double the daily dose in a few days, if necessary, with complete safety. In convalescence one has to be ready to reduce the dose rapidly to the original level as soon as blue tests reappear. Gastro-intestinal distur-

bances are far more troublesome. It is dull, but easy, to take the day's carbohydrate at the right times in the form of glucose. Any diabetic should be able to do this unaided until he can once more take the normal diet. If he cannot even take glucose he must go to hospital immediately.

One of the problems for which each diabetic must find his own solution is that of deciding whether to conceal his condition or to admit it freely. My own solution is to be fairly frank about it. Diabetes is widely believed to be a serious disability and is so regarded by many employers, so I like to advertise the complete normality of my life. I have found even professional colleagues surprised to find no apparent evidence of restriction in my activities. I do not mean that I go everywhere with a boring story of my diabetes, but I make no effort to conceal my reason for refusing some offered dish, for suddenly eating sugar or for excusing myself to give an injection. It may even be dangerous to make a complete secret of diabetes as some patients do. They may be overtaken by illness or hypoglycæmia, and the doctor who is summoned will be handicapped if he does not know that his, perhaps unconscious, patient is a diabetic.

(5) DIABETIC MATURITY

This is a state that is probably never reached. I am still learning new tricks of the trade to cope with new situations, but I have reached a pretty steady level of insulin dosage, and I find dietetics are now the activity of some almost unconscious part of my mind. My anxieties are few and I seldom experience any hesitant anxiety when I go for an uncivilized holiday or spend a long day away from home, with the prospect of irregular meals. There are risks, however, in the mere feeling of confidence and familiarity. Once or twice a year, usually because of some disturbance of the morning routine, I forget my morning dose of insulin. Profuse polyuria in the middle of the morning reminds me, and the normal dose taken then, with rather a smaller lunch and larger tea, corrects the error. I have learnt to keep a syringe and some insulin in my car and at the office against this eventuality. I have once gone for a remote holiday and found I had left both insulin and syringe behind. This led to an annoying waste of petrol in driving miles to the nearest hospital. Now I automatically murmur: "Insulin, syringe, sugar" when I pack for even a single night away from home. I always put one syringe and phial in my pocket and pack a second in my case.

The future is full of confidence. The experience of those old-established diabetics who have been taking insulin for twenty-five years shows how little there is to fear. The present is full of gratitude to medical science for the good health that I have had ensured, but it is also tinged with regret that so many diabetics have not learnt to live a full and normal life. Medical science has given them insulin but the medical profession has not given them the education they need. The general practitioner, with perhaps only one or two diabetic patients, cannot be asked to undertake this. Diabetic clinics must be made available throughout the country and education of the diabetic must take equal place with the prescription of diet and insulin.

diet. A diabetic who is living a normal social life must meet occasions when it is impossible to estimate carbohydrate accurately. It is therefore necessary to err on the generous side and be undismayed if heavy glycosuria results.

Perhaps the most important lesson I learnt during this period was that hypoglycæmic symptoms are constantly changing. At first my symptoms were those due to adrenaline action—sweating, tremor and palpitation—quite characteristic and easy to recognize. After a few months, these gave way to ocular symptoms—dimness of vision and occasional diplopia. Emotional symptoms finally became more prominent—irritability or hilarity. These are more easily recognized by my wife than by myself (I have learnt the wisdom of taking sugar on her advice, even when I see no need myself). The symptoms are occasionally very indefinite; just a vague feeling of uneasiness for which I have to keep a careful watch at the times of maximum insulin action.

I took a mixture of protamine zinc and soluble insulin at first, but after a time I found it inconvenient and have changed to two doses of ordinary insulin. The reason is that a dose of P.Z.I. demands that tea and supper should be taken at the correct time. It is no pleasure (as was once my lot) to eat sugar throughout a performance at the theatre and to be unable to join the rest of the party at supper afterwards. Breakfast and lunch are fixtures in nearly everyone's life and can cover the morning dose of soluble insulin. Tea can be dispensed with and supper is a movable feast and can be much more easily covered by an evening dose taken just before the meal. I make it a rule to take the evening dose immediately before supper. It is unwise, when going out to supper, to take the dose at home before starting: I have once done this and been in difficulties when the lateness of a fellow guest delayed the meal for an hour. Moreover, there is always the risk of delay, or even an accident, on the journey to a meal away from home. There is never any difficulty in asking to "wash one's hands" before the meal in order to give the injection.

During this period a diabetic will probably experience his first attack of a cold or "flu", which will almost certainly demand a large increase of insulin requirement. It was during my first experience of a bout of influenza after I became diabetic that I fully realized the advantage of my medical training, in that I was not afraid to increase my insulin boldly. How little teaching would be necessary to enable any intelligent diabetic to do this! Frequent urine testing is, of course, the secret. I adopt four-hourly testing. I take my normal dose of insulin and then give myself an extra six units of insulin after each "red" test, and keep glucose handy in case of any suspicion of hypoglycæmia. On the second day I add on to the morning dose the total number of extra units that I had to take on the first day and on to the evening the extra units I required the previous evening. In this way it is possible to double the daily dose in a few days, if necessary, with complete safety. In convalescence one has to be ready to reduce the dose rapidly to the original level as soon as blue tests reappear. Gastro-intestinal distur-

constantly in areas long associated with fibrositis and they spoke of the "basic fat pattern" to be found in these areas. They suggest that localized collections of fat lying under fascial planes or along certain tendon sheaths, may, in certain circumstances, become œdematous, cause tension and give rise to the pain of "fibrositis". From their work it would appear that the "fibrositic nodule" so beloved of the physiotherapist, is in fact a fatty mass, which can be "broken down" by sufficient trauma, such as by hard, deep massage.

The syndrome of fibrositis typically affects certain definite areas. It is commonly found to affect the lower back, the glutei, the shoulder girdles, and the neck. In these areas are found muscles thickly invested with fibrous tissue or separated from other muscles by fibrous septa or connected with short, thick, fibrous tendons. Such areas, too, may be associated with the "basic fat pattern" described by Copeman. It is thus necessary to attempt to collate accepted etiology with anatomical structure and form a pathological picture which fits in with both. At the same time it will be of value to consider the muscular stiffness which occurs after unaccustomed exercise, for this presents in a similar way to fibrositis, being associated with pain and stiffness in muscles or muscle groups.

To take first the pain of muscular stiffness; this occurs when muscles which have been subjected only to incidental activity are suddenly exercised strongly. After a period of rest, renewed activity causes pain and stiffness which is "worked off" after further exercise. Many suggestions have been made to account for this painful stiffness; among other causes, rupture of small fibres and the presence of "toxins" have been blamed. If, however, a muscle in a state of relative physiological inactivity and hypotonia is put into violent activity, it is easy to picture the change that will take place in that muscle. There will be great and unaccustomed hyperæmia, probably associated with actual micro-trauma to some of its resting, inelastic fibres. This will result in exudation of lymph and serum between the muscle fibres, which in turn will lead to tension; renewed activity and contraction will increase the tension and cause pain and reflex "stiffness". But in the large muscle groups, such as the hamstrings and quadriceps where stiffness occurs, there are no firm fascial sheaths and the tissue is relatively free and unrestricted; thus exudates can readily be squeezed on in the healthy subject. Renewed activity thus relieves the tension and stiffness of unaccustomed muscular activity.

In fibrositic areas relief will not be so easily obtained; here fascial sheaths will be submitted to tension and will hold in the exudates. The pain will be more severe and the reflex stiffness so marked that the patient may speak of "locking", and be reduced to complete immobility, as occurs in an acute attack of lumbago or lumbar fibrositis. That cold, extremes of temperature and draughts can affect the local circulation is known. A part may become "blue and swollen with cold"; this means that there is a vascular stasis and

FIBROSITIS

By WILLIAM TEGNER, B.M., M.R.C.P.

*Physician-in-Charge, Department of Physical Medicine, the London Hospital;
Physician, the British Red Cross Society's Clinic for Rheumatism, London.*

IT has been said that a general practitioner spends ten per cent. of his time
treating "rheumatism". Of this rheumatism, arthritis will account for a
certain proportion but much of the rest will be regarded and treated as
"fibrositis". Fibrositis is a convenient label for many of the aches and pains
which affect the locomotor system, but it should not be allowed to become a
mere diagnostic refuge and should connote a definite syndrome and patho-
logical picture. Without such an objective attitude towards the condition,
treatment and prognosis become mere guess-work.

PATHOGENESIS

Fibrositis (including fibromyositis) is a painful condition affecting the
fibrous tissue of muscles, fascial planes, intramuscular septa and peri-
articular tissues.

Infection is believed to play an important part in the pathogenesis of
fibrositis, but the direct infective theory originally propounded by Stockman
(1920) receives little support. He himself said that the reaction to the
bacterial invasion was not polymorphonuclear but lymphocytic, and as he
could not demonstrate the bacteria he suggested that they were rapidly
destroyed. Such a concept of acute and transient local, non-specific bac-
terial invasion without polymorphonuclear response is not favoured by
morbid anatomists. On the other hand, there is a school of thought which
ascribes the local changes of fibrositis to the toxins secreted by foci of
infection elsewhere in the body, which are able to set up chronic inflamma-
tory changes in remote areas which are poorly supplied with blood vessels.
This concept, once almost universally supported, is now losing popularity.
That cold, chill, damp, change in the weather and trauma can act as triggers
which start an attack of fibrositis seems to have the support of tradition and
popular experience.

Two more recent contributions to the pathology of fibrositis need con-
sideration. It has been shown by Elliott (1944a), among other workers, that
areas of muscle spasm can occur due to irritation of nerves at some more
central point, and that these areas of muscle spasm when subjected to
pressure can cause radiation of pain. Copeman and Ackermann (1944)
reported a series of biopsies performed on patients suffering from fibrositis
in which they excised trigger areas which gave rise to so-called fibrositic pain.
In all their cases they were able to demonstrate subfascial protrusions of fat,
either bulging under the fascia, protruding through it or actually pedun-
culated through foramina. These herniations and bulgings were found

eradication of appendages, such as teeth or tonsils, as completely unjustified and a purely speculative manœuvre in treatment.

In certain cases fibrositis seems to follow generalized infection. This does not necessarily demand a "toxic" origin. It can readily be argued that decubitus and metabolic change can lead to subfascial exudate and tension and that such tension can bring to the fore pre-existing areas of subfascial fatty nodules.

DIAGNOSIS

Acute fibrositis comes on suddenly without prodromal symptoms, sometimes after exposure to cold, damp or variation of temperature. It sometimes follows strain or exertion. It is characterized by localized pain aggravated by movement and relieved by rest and warmth. The pain on movement varies in intensity but may be severe and incapacitating. Examination will reveal no generalized constitutional disturbances, such as fever, but localized pain on pressure in certain muscles and muscle groups. The muscles will be tense and may stand out in spasm. There may be deep areas of increased tension which are very painful on firm palpation. These painful areas will coincide with the anatomical picture of the affected muscles. Diagnosis is not usually difficult in acute fibrositis. The history of the sudden onset, possibly of previous attacks, the lack of signs of generalized disease and the localized tenderness are usually sufficient to establish the identity of the condition. It is always advisable to inquire into the urinary history and to test the urine, as renal conditions may sometimes cause diagnostic difficulty in cases of backache. Occasionally fibrositis may ape an abdominal emergency, but here again the lack of general constitutional symptoms is usually sufficient to eliminate the more serious condition.

Chronic fibrositis may follow on an acute attack or may arise insidiously. The pain is less severe but more persistent than in the acute condition. It is relieved by rest and warmth but is aggravated after rest, and the patient complains of pain and stiffness on getting up in the mornings or after resting in a chair. Movement is then painful but the patient learns to "work it off"; with activity there may be complete relief until after a further period of rest. There may be recurrent exacerbations and ameliorations and the patient may find the fibrositis reacts to changes of weather and domicile. It is possible that changes of weather exert their influence through changes in local barometric pressure within the tense areas.

The differential diagnosis of chronic fibrositis is more difficult than that of the acute form. First, neuritides may present difficulty, but in these the pain is more severe and persistent and is not as a rule relieved by rest; in fact it is often aggravated and the patient suffers more severely when warm in bed. Tenderness is greater along the nerve trunk than in the muscles supplied by it and the pain has the anatomical distribution of the nerve trunk. There may be muscular wasting, diminution of tendon-jerks and sensory changes.

exudation, and in certain areas exudate can lead to painful tension. Moreover, if subfascial collections of fat are present in these areas any increased tension will be aggravated by them. This fact was noted by Pugh and Christie (1945), who found that subfascial nodules could be found in a definite percentage of all the subjects they examined, but that in those with a previous history of "rheumatism" they were ten times more likely to be tender on palpation than in those who gave no such history. In a more recent paper, Copeman and Pugh (1945) have demonstrated that by dehydrating patients suffering from fibrositis they can temporarily relieve the pain. They believe this to be due to a withdrawal of water which has been held in combination with the subfascial collections of fat; it is equally possible that dehydration of underlying muscle will reduce its volume and ease tension. This would fit in with the relief felt by some sufferers from fibrositis when they experience a febrile illness associated with much sweating.

Here then is a picture of the acute attack of fibrositis; the exudation leading to increased tension, and tension leading to pain and reflex stiffness. If this exudate is worked off by purposeful muscular activity or squeezed on by physiotherapy, the attack may pass off. If, on the other hand, the reflex stiffness causes the subject to interrupt muscular activity, the exudate will not be rapidly absorbed and may go on to reproduce the pathological changes of unabsorbed tissue fluid. There will be a proliferation of fibroblasts and the laying down of fresh fibrous tissue; the muscles in that area will then become invested and bound by more fibrous tissue than is normal. This will mean an increase in tension on activity, more pain on movement, and either a greater liability to further acute attacks of fibrositis or the setting up of a state of chronic fibrositis when, owing to thickening, shortening and tension of fibrous tissue, all movement becomes painful. A vicious circle has been set up, and any subfascial fat is in an increased state of tension.

FIBROSITIS AND INFECTION

The relationship between infection and fibrositis remains a source of much controversy. That general infections can cause aching and pain in muscles is well known; a common instance of this is the aching in the limbs which is so often associated with influenza. Some would describe this pain as a toxic fibromyositis. Others would ascribe the local manifestations of acute and chronic fibrositis to toxins elaborated at some focus of infection, such as an infected tonsil or an apical tooth abscess. Such a concept has never been disproved, and occasionally good results are found when foci of chronic infection are treated. On the other hand, it seems impossible to demonstrate the concept of localized action of a toxin elaborated from a distant, non-specific focus of infection on a basis of morbid histology. All who treat chronic rheumatic infections are aware of the disappointments that may result from a painstaking search for, and eradication of, infected foci as a method of treating fibrositis. Most workers now consider the wholesale

eradication of appendages, such as teeth or tonsils, as completely unjustified and a purely speculative manœuvre in treatment.

In certain cases fibrositis seems to follow generalized infection. This does not necessarily demand a "toxic" origin. It can readily be argued that decubitus and metabolic change can lead to subfascial exudate and tension and that such tension can bring to the fore pre-existing areas of subfascial fatty nodules.

DIAGNOSIS

Acute fibrositis comes on suddenly without prodromal symptoms, sometimes after exposure to cold, damp or variation of temperature. It sometimes follows strain or exertion. It is characterized by localized pain aggravated by movement and relieved by rest and warmth. The pain on movement varies in intensity but may be severe and incapacitating. Examination will reveal no generalized constitutional disturbances, such as fever, but localized pain on pressure in certain muscles and muscle groups. The muscles will be tense and may stand out in spasm. There may be deep areas of increased tension which are very painful on firm palpation. These painful areas will coincide with the anatomical picture of the affected muscles. Diagnosis is not usually difficult in acute fibrositis. The history of the sudden onset, possibly of previous attacks, the lack of signs of generalized disease and the localized tenderness are usually sufficient to establish the identity of the condition. It is always advisable to inquire into the urinary history and to test the urine, as renal conditions may sometimes cause diagnostic difficulty in cases of backache. Occasionally fibrositis may ape an abdominal emergency, but here again the lack of general constitutional symptoms is usually sufficient to eliminate the more serious condition.

Chronic fibrositis may follow on an acute attack or may arise insidiously. The pain is less severe but more persistent than in the acute condition. It is relieved by rest and warmth but is aggravated after rest, and the patient complains of pain and stiffness on getting up in the mornings or after resting in a chair. Movement is then painful but the patient learns to "work it off"; with activity there may be complete relief until after a further period of rest. There may be recurrent exacerbations and ameliorations and the patient may find the fibrositis reacts to changes of weather and domicile. It is possible that changes of weather exert their influence through changes in local barometric pressure within the tense areas.

The differential diagnosis of chronic fibrositis is more difficult than that of the acute form. First, neuritides may present difficulty, but in these the pain is more severe and persistent and is not as a rule relieved by rest; in fact it is often aggravated and the patient suffers more severely when warm in bed. Tenderness is greater along the nerve trunk than in the muscles supplied by it and the pain has the anatomical distribution of the nerve trunk. There may be muscular wasting, diminution of tendon-jerks and sensory changes.

exudation, and in certain areas exudate can lead to painful tension. Moreover, if subfascial collections of fat are present in these areas any increased tension will be aggravated by them. This fact was noted by Pugh and Christie (1945), who found that subfascial nodules could be found in a definite percentage of all the subjects they examined, but that in those with a previous history of "rheumatism" they were ten times more likely to be tender on palpation than in those who gave no such history. In a more recent paper, Copeman and Pugh (1945) have demonstrated that by dehydrating patients suffering from fibrositis they can temporarily relieve the pain. They believe this to be due to a withdrawal of water which has been held in combination with the subfascial collections of fat; it is equally possible that dehydration of underlying muscle will reduce its volume and ease tension. This would fit in with the relief felt by some sufferers from fibrositis when they experience a febrile illness associated with much sweating.

Here then is a picture of the acute attack of fibrositis; the exudation leading to increased tension, and tension leading to pain and reflex stiffness. If this exudate is worked off by purposeful muscular activity or squeezed on by physiotherapy, the attack may pass off. If, on the other hand, the reflex stiffness causes the subject to interrupt muscular activity, the exudate will not be rapidly absorbed and may go on to reproduce the pathological changes of unabsorbed tissue fluid. There will be a proliferation of fibroblasts and the laying down of fresh fibrous tissue; the muscles in that area will then become invested and bound by more fibrous tissue than is normal. This will mean an increase in tension on activity, more pain on movement, and either a greater liability to further acute attacks of fibrositis or the setting up of a state of chronic fibrositis when, owing to thickening, shortening and tension of fibrous tissue, all movement becomes painful. A vicious circle has been set up, and any subfascial fat is in an increased state of tension.

FIBROSITIS AND INFECTION

The relationship between infection and fibrositis remains a source of much controversy. That general infections can cause aching and pain in muscles is well known; a common instance of this is the aching in the limbs which is so often associated with influenza. Some would describe this pain as a toxic fibromyositis. Others would ascribe the local manifestations of acute and chronic fibrositis to toxins elaborated at some focus of infection, such as an infected tonsil or an apical tooth abscess. Such a concept has never been disproved, and occasionally good results are found when foci of chronic infection are treated. On the other hand, it seems impossible to demonstrate the concept of localized action of a toxin elaborated from a distant, non-specific focus of infection on a basis of morbid histology. All who treat chronic rheumatic infections are aware of the disappointments that may result from a painstaking search for, and eradication of, infected foci as a method of treating fibrositis. Most workers now consider the wholesale

easier by the fact that there is often some organic basis for the pain which is heavily obscured by functional symptoms. In predominantly psychogenic pain the history is normally indirect, long-winded and full of bizarre terms. The description of the intensity, causation, aggravation and distribution of the pain does not fit in with any pathological or anatomical picture. Examination will frequently evoke an hysterical over-reaction and an extreme general difficulty in relaxation. Sympathetic and vigorous treatment directed at some area where there is possibly an underlying organic lesion may result in the relief of local symptoms with their reappearance elsewhere. The care and attention devoted to the sufferer from psychogenic pain may be most welcome and most reluctantly given up. On the other hand, the mere absence of physical signs associated with rheumatic pain is not, in itself, a justification for the diagnosis of psychogenic pain. Flind and Barber (1945) have pointed out that there must be real evidence of psychological distur-bance before such a diagnosis can be made.

TREATMENT

In *acute fibrositis* a speedy and effective therapeutic procedure is desirable, not only to relieve the sufferer but also to prevent the condition becoming chronic. Rest, heat and analgesics alone are often effective, but traditionally massage is added to these to hasten the process of recovery. Such treatment is physiologically sound in that rest relieves the pain, heat increases the local circulation and aids in the absorption of exudates and also soothes the pain, whilst massage mechanically squeezes on the exudates and prevents the laying down of fresh fibrous tissue. Such treatment, however, has the disadvantage of taking time and of being expensive if a physiotherapist is employed. Thus rest, analgesics and the domestic forms of heat, such as the hot-water bottle, are often employed with considerable success.

Recently the use of injections of a local anæsthetic has proved of value and such treatment is now extensively used. The different schools of thought on the pathological basis of fibrositic pain are in agreement on the value of local anæsthetics. Thus both Elliott, who believes that muscle spasm due to nerve irritation is responsible for much pain which is labelled fibrositic, and Copeman and Ackermann, who discovered the part played by fat protrusion, agree that this procedure alleviates the pain. Copeman thinks that the injec-tion acts not merely by its anæsthetic action but that the introduction of fluid breaks up the collection of fat; he advocates subcutaneous teasing with a surgical needle as a means of treatment. It seems that in cases in which fat protrusion exists the prime objective is to break it up and this can be done either by the skilled technique of deep massage, by bursting the fat lobules, by the injection into them of fluid, or by teasing them with a sharp surgical needle; all of these procedures would relieve the tension caused by the pressure of œdema on the fat and by the fat on the fibrous tissue. In acute fibrositis, such as that of the lumbar muscles, when "nodules" cannot be

Arthritis of joints underlying the muscles must be eliminated as a cause of pain. In the weight-bearing joints, such as the hip or knee, this is not usually difficult, as the history will be of pain when weight is placed on the joint, and clinical and radiological examination will reveal the arthritis. But in the intervertebral and sacro-iliac joints the differentiation may not be so easy. At this point it should be stressed that after middle age a certain degree of osteophytic outgrowth and bony marginal reaction is common in these joints and *is frequently quite symptomless*. It is unjustifiable to ascribe all or any symptoms which may have occurred to an osteoarthritis of the spine which has been reported on radiological examination. A careful clinical history and examination are needed. When pain is due to intervertebral osteoarthritis it is usually due to pressure on nerve roots and can be anatomically correlated with them; when pain is due to sacro-iliac strain or arthritis it is usually referred directly to these joints, and manipulation of these joints aggravates the pain. It must always be borne in mind that fibrositis may coincide with chronic arthritic changes, and a successful treatment of the fibrositis may reveal that the arthritis is symptomless.

Careful clinical and radiological evidence will be needed for the elimination of such rarer conditions as spondylolisthesis. In women the decision often has to be made whether low backache is fibrositic in origin or due to intra-pelvic causes. *Intra-pelvic disorders* may well present symptoms of low back pain. But in these conditions the history is usually of an onset of pain connected with some gynæcological condition, such as a difficult labour or pelvic infection; the pain does not normally present typical fibrositic characteristics and may be aggravated by menstruation. Sacro-iliac strain may be initiated by difficult labour, but here the typical pain can usually be elicited by manipulating the sacro-iliac joints. It must, however, be remembered that true fibrositis may be present, as well as an intra-pelvic condition; moreover, the period of decubitus associated with child-birth or a pelvic infection may initiate a fibrositis. Many cases of fibrositis in women are regarded as manifestations of intra-pelvic disturbance and the converse is equally true, for many cases of intra-pelvic disturbance are regarded as being fibrositic.

The syndrome produced by *herniation of an intervertebral* disc may simulate fibrositis and, as Elliot (1944b) has pointed out, may be mistaken for it. He described tenderness in muscles due to prolapsed discs; in the case of the glutei this may easily simulate fibrositis. Here the anatomical picture differs from typical fibrositis, symptoms being those of root pain and not of muscular tension, and there should be radiological evidence of disc herniation.

Finally, and by no means least in importance, there is frequently the problem of whether or not the pain of which the patient is complaining is not largely psychogenic. *Psychogenic pain* frequently mimics the various types of rheumatism and the problem of differentiation is not made any

easier by the fact that there is often some organic basis for the pain which is heavily obscured by functional symptoms. In predominantly psychogenic pain the history is normally indirect, long-winded and full of bizarre terms. The description of the intensity, causation, aggravation and distribution of the pain does not fit in with any pathological or anatomical picture. Examination will frequently evoke an hysterical over-reaction and an extreme general difficulty in relaxation. Sympathetic and vigorous treatment directed at some area where there is possibly an underlying organic lesion may result in the relief of local symptoms with their reappearance elsewhere. The care and attention devoted to the sufferer from psychogenic pain may be most welcome and most reluctantly given up. On the other hand, the mere absence of physical signs associated with rheumatic pain is not, in itself, a justification for the diagnosis of psychogenic pain. Flind and Barber (1945) have pointed out that there must be real evidence of psychological disturbance before such a diagnosis can be made.

TREATMENT

In *acute fibrositis* a speedy and effective therapeutic procedure is desirable, not only to relieve the sufferer but also to prevent the condition becoming chronic. Rest, heat and analgesics alone are often effective, but traditionally massage is added to these to hasten the process of recovery. Such treatment is physiologically sound in that rest relieves the pain, heat increases the local circulation and aids in the absorption of exudates and also soothes the pain, whilst massage mechanically squeezes on the exudates and prevents the laying down of fresh fibrous tissue. Such treatment, however, has the disadvantage of taking time and of being expensive if a physiotherapist is employed. Thus rest, analgesics and the domestic forms of heat, such as the hot-water bottle, are often employed with considerable success.

Recently the use of injections of a local anæsthetic has proved of value and such treatment is now extensively used. The different schools of thought on the pathological basis of fibrositic pain are in agreement on the value of local anæsthetics. Thus both Elliott, who believes that muscle spasm due to nerve irritation is responsible for much pain which is labelled fibrositic, and Copeman and Ackermann, who discovered the part played by fat protrusion, agree that this procedure alleviates the pain. Copeman thinks that the injection acts not merely by its anæsthetic action but that the introduction of fluid breaks up the collection of fat; he advocates subcutaneous teasing with a surgical needle as a means of treatment. It seems that in cases in which fat protrusion exists the prime objective is to break it up and this can be done either by the skilled technique of deep massage, by bursting the fat lobules, by the injection into them of fluid, or by teasing them with a sharp surgical needle; all of these procedures would relieve the tension caused by the pressure of œdema on the fat and by the fat on the fibrous tissue. In acute fibrositis, such as that of the lumbar muscles, when "nodules" cannot be

felt, the action of a local anæsthetic must be somewhat different. Here the effect of local anæsthesia is to relieve the pain and abolish the reflex stiffness brought about by the pain. The sufferer can then move in comfort, movement of the muscle will result in increase of circulation and a squeezing out of exudate, and also in stretching of fibrous tissue and in prevention of the formation of new areas of shortened, thickened fibrous tissue. This action would be assisted by massage and enhanced by active movement.

The technique to be adopted may vary in detail. Certain points in the use of local anæsthesia for fibrositis will bear description.

The area or areas to be injected should be chosen with care. Points of maximum tenderness should be found, and in particular "trigger points" from which the pain radiates on firm palpation. These will often be found to coincide with subfascial "nodules" which are probably fatty in structure. For the comfort of the patient and the ease of the operation, the skin over the area to be injected should always be anæsthetized with a watery solution of 2 per cent. novocain. For the deeper injection a bigger needle is used and it is my practice to use a solution of 1.5 per cent. procaine in oil. The oily solution is absorbed much more slowly than a watery solution and allows of a more prolonged anæsthetic action. Through the anæsthetized skin the needle can be moved from point to point through a fairly wide radius without discomfort to the patient. Occasionally the patient will find that at certain spots the injection is eliciting pain; this should be regarded as an encouraging sign that the needle has struck the area of tension and the injection should be continued to break down any fibrosis. Usually 5 c.cm. of solution is sufficient for each injection; but multiple injections may have to be given. Immediately after the injection there should be relief of pain and the patient should be encouraged to go through a full range of movements. This will not only demonstrate to the patient the relief of symptoms but by muscular activity will disseminate the anæsthetic fluid, re-establish normal circulation and prevent contracture. A routine course of simple active exercise should always be prescribed after local injection.

In *chronic fibrositis* satisfactory treatment may often demand considerable perseverance and patience, both from the sufferer and from the physician. It must be stressed that cases of chronic fibrositis which clear up quickly under treatment are the exception rather than the rule; the prescription of one short course of physiotherapy may well be useless and disappointing and it should be made clear to the patient that the restoration of normal painless function will take time. Physiotherapy has a traditional and accepted place in the treatment of chronic fibrositis. It is most commonly prescribed in the form of heat and massage; to this, active movement should be added in every case.

·Heat can be prescribed in a number of forms. Radiant heat, employing the shorter, more penetrating rays of the infra-red spectrum, is often most efficacious. Similarly, the non-luminous infra-red rays exert a valuable superficial heating effect with reflex deep vasodilatation. Diathermy, whether long- or short-wave, also produces a valuable heat, in this instance generated in the tissues themselves. All these forms of heat have the effect of increasing local blood supply, softening fibrous tissue and soothing pain. Added to heat, massage aids in the increase of circulation, forces exudate into the circulation, can break down the looser adhesions of fresh fibrous tissue,

and if deep and persevering can break up "nodules" of subfascial fat. To stop at this is unjustified and may be disappointing, for complete rest and relaxation after such treatment may allow of the restoration of the pathological condition. When relieved by treatment the patient, under the expert guidance of an understanding physiotherapist, must go actively through a range of movements to maintain the improvement that has been gained and to regain confidence that painless movement can be restored. To prescribe purely passive physiotherapy, in which the patient makes no personal effort at restoring function, is unwise and may prolong disability. It is sometimes necessary to change the form in which heat has been prescribed during treatment. A temporary exacerbation of symptoms on the initiation of treatment is not of adverse significance, as measures to break up the fibrous tissue may be painful. But if the expected response is not forthcoming, a change from radiant heat to diathermy or *vice versa* often produces the desired effect.

The use of local injections in chronic fibrositis is often valuable; these may have to be widespread and repeated, and may have to be used in conjunction with physiotherapy. The response will not be as dramatic as in acute fibrositis, and in certain doubtful cases in which there may be a preponderating psychogenic factor in the pain, the effect of local injections will demonstrate this fact in a striking manner. A small local injection of 2 per cent. novocain into the *erector spinæ* once evoked the following startling response : " Your injection cured my backache but paralysed my bowels, and I have had to have colonic lavage ever since". On the whole, the longer symptoms have existed, the less satisfactory the prognosis will be for the use of local injections.

The problem of treatment in a patient whose symptoms are adjudged to be partly or largely psychogenic is a very real one. If the greater part of the pain is considered to be functional, the greater part of the treatment must be psychological. In fibrositis overlaid by psychogenic factors a combination of organic and psychotherapeutic procedure is indicated. The general practitioner is usually an excellent judge of his patient's mental condition, and is often able to allay fear, to explain and to reassure with good results. Flind and Barber (1945) have found that in intelligent patients "psychogenic rheumatism" can often be relieved by such means.

The use of drugs in the treatment of fibrositis can be dismissed briefly. No drug is known which can cure the condition. Drugs are used merely in the treatment of the symptoms. Salicylates may be useful as mild analgesics, but there is no evidence that they have any direct influence on the pathological condition. The same can be said of the iodides.

The treatment of *infective foci* found in association with fibrositis needs careful consideration. If infection of teeth or tonsils is found in the sufferer from fibrositis, it should be explained that this pathological condition exists, that its eradication may or may not help the fibrositis, but that to establish

felt, the action of a local anæsthetic must be somewhat different. Here the effect of local anæsthesia is to relieve the pain and abolish the reflex stiffness brought about by the pain. The sufferer can then move in comfort, movement of the muscle will result in increase of circulation and a squeezing out of exudate, and also in stretching of fibrous tissue and in prevention of the formation of new areas of shortened, thickened fibrous tissue. This action would be assisted by massage and enhanced by active movement.

The technique to be adopted may vary in detail. Certain points in the use of local anæsthesia for fibrositis will bear description.

The area or areas to be injected should be chosen with care. Points of maximum tenderness should be found, and in particular "trigger points" from which the pain radiates on firm palpation. These will often be found to coincide with subfascial "nodules" which are probably fatty in structure. For the comfort of the patient and the ease of the operation, the skin over the area to be injected should always be anæsthetized with a watery solution of 2 per cent. novocain. For the deeper injection a bigger needle is used and it is my practice to use a solution of 1.5 per cent. procaine in oil. The oily solution is absorbed much more slowly than a watery solution and allows of a more prolonged anæsthetic action. Through the anæsthetized skin the needle can be moved from point to point through a fairly wide radius without discomfort to the patient. Occasionally the patient will find that at certain spots the injection is eliciting pain; this should be regarded as an encouraging sign that the needle has struck the area of tension and the injection should be continued to break down any fibrosis. Usually 5 c.cm. of solution is sufficient for each injection; but multiple injections may have to be given. Immediately after the injection there should be relief of pain and the patient should be encouraged to go through a full range of movements. This will not only demonstrate to the patient the relief of symptoms but by muscular activity will disseminate the anæsthetic fluid, re-establish normal circulation and prevent contracture. A routine course of simple active exercise should always be prescribed after local injection.

In *chronic fibrositis* satisfactory treatment may often demand considerable perseverance and patience, both from the sufferer and from the physician. It must be stressed that cases of chronic fibrositis which clear up quickly under treatment are the exception rather than the rule; the prescription of one short course of physiotherapy may well be useless and disappointing and it should be made clear to the patient that the restoration of normal painless function will take time. Physiotherapy has a traditional and accepted place in the treatment of chronic fibrositis. It is most commonly prescribed in the form of heat and massage; to this, active movement should be added in every case.

·Heat can be prescribed in a number of forms. Radiant heat, employing the shorter, more penetrating rays of the infra-red spectrum, is often most efficacious. Similarly, the non-luminous infra-red rays exert a valuable superficial heating effect with reflex deep vasodilatation. Diathermy, whether long- or short-wave, also produces a valuable heat, in this instance generated in the tissues themselves. All these forms of heat have the effect of increasing local blood supply, softening fibrous tissue and soothing pain. Added to heat, massage aids in the increase of circulation, forces exudate into the circulation, can break down the looser adhesions of fresh fibrous tissue,

SOME ASPECTS OF WRIST INJURIES IN ELDERLY PATIENTS

By D. LL. GRIFFITHS, M.B.E., F.R.C.S.

THE subject of injuries about the wrist joint, and especially in elderly patients, is of topical interest at this time of year, for the wrist is particularly vulnerable in winter. Icy pavements and dark staircases take a heavy toll, and a few notes on the more common injuries of this region may be helpful.

THE "SPRAINED WRIST"

It is still inadequately realized that, apart from quite trivial injuries, the most frequent result of injury in the region of the wrist is a fracture. Moreover, the majority of these fractures are undisplaced, or insufficiently displaced to produce visible deformity. They are therefore easily overlooked and the possibly disastrous effects of their neglect will continue until every practitioner is aware that a genuine "sprained wrist" is a rare occurrence. The facile diagnosis of "sprain" has meant failure to recognize many fractured carpal scaphoids in young adults and, in older people, the so-called sprain is all too often an impacted fracture of the lower end of the radius. The potential legal consequences of mistaking a fracture for a sprain are illustrated by the annual pleas of the Medical Defence Societies for routine X-ray examination of injured joints, and these pleas are peculiarly appropriate in connexion with the wrist. *If a wrist injury is severe enough to make the patient seek medical advice, it is severe enough to require an X-ray examination* and, to be adequate, the films must include antero-posterior, lateral and oblique views. If good X-ray films, exposed in these three planes, do not show any fracture, the provisional diagnosis of sprain or of contusion is permissible, but it should still be made with reserve. Should symptoms persist after ten or fourteen days, there should be no hesitation in repeating the X-ray examination, as the passage of one or two weeks may make a fracture line more obvious.

Severely sprained wrists are liable to be painful for a surprisingly long time, and this is particularly true of the injuries of the elderly. It is therefore no bad plan to treat such sprains by *splintage*, however normal the X-ray appearances. The best splint to use, even in old patients, is a light plaster cast, a "cock-up" plaster (fig. 7), and a short period of fixation in such a cast will give the damaged tissues their best chance of repair and will prevent many such sprains from becoming chronic. Naturally, prolonged fixation is not advised; two to three weeks should be ample, and a word of warning about the use of plaster of Paris in such injuries is necessary. Properly applied, there is no better splint, but the application is not easy.

sound bodily health in order to combat the fibrositic process the eradication of infected foci is advisable. Vaccines of a great variety are often prescribed for fibrositis; these may be "stock vaccines" or may be prepared from foci of infection. Although some claim success from their use, it is difficult to understand how they act; for even in pathological conditions of known etiology, vaccines of the causative organism are useless as a form of treatment. Vaccines injected locally into painful areas are sometimes claimed to be efficacious. But here we are faced with the fact that the injection of *any fluid* into such lesions as a fatty nodule is known to be effective in breaking it down.

Finally, the value of treatment at a spa must be considered. Spas offer various forms of hydrotherapy and much more. That various sprays and douches can cause hyperæmia is well established; such treatment may therefore be of value in fibrositis. Moreover, mineral spas can offer the opportunity of exercise in waters of high density and therefore make movements easier than in air. But all spas are equipped with extensive facilities for physiotherapy and this can be prescribed in great detail and variety. What is even more important is that the patient who goes to a spa for treatment goes there with the definite object in view of devoting his whole time to a "cure". He is therefore willing to accept a regime of treatment and not merely to spare an occasional hour from his everyday activities. Spa treatment can thus be of great value and, if economic circumstances permit, may ensure a rapid relief of symptoms and a cure of fibrositis.

CONCLUSION

Fibrositis is a condition with a definite pathological picture, presenting a typical syndrome and responsive to certain measures of treatment. It should not be diagnosed except after careful clinical examination and the term should not be used as a loose synonym for locomotor pain.

References

Copeman, W. S. C., and Ackermann, W. L. (1944): *Quart. J. Med.*, **13**, 37.
——, and Pugh, L. G. C. E. (1945): *Lancet*, ii, 553.
Elliott, F. A. (1944a): *Ann. Rheum. Dis.*, 4, 22.
—— (1944b): *Lancet*, i, 47.
Flind, J., and Barber, H. S. (1945): *Quart. J. Med.*, **14**, 57.
Pugh, L. G. C. E., and Christie, T. A. (1945): *Ann. Rheum. Dis.*, **5**, 8.
Stockman, R. (1920): "Rheumatism and Arthritis," Edinburgh.

SOME ASPECTS OF WRIST INJURIES IN ELDERLY PATIENTS

By D. LL. GRIFFITHS, M.B.E., F.R.C.S.

THE subject of injuries about the wrist joint, and especially in elderly patients, is of topical interest at this time of year, for the wrist is particularly vulnerable in winter. Icy pavements and dark staircases take a heavy toll, and a few notes on the more common injuries of this region may be helpful.

THE ''SPRAINED WRIST''

It is still inadequately realized that, apart from quite trivial injuries, the most frequent result of injury in the region of the wrist is a fracture. Moreover, the majority of these fractures are undisplaced, or insufficiently displaced to produce visible deformity. They are therefore easily overlooked and the possibly disastrous effects of their neglect will continue until every practitioner is aware that a genuine "sprained wrist" is a rare occurrence. The facile diagnosis of "sprain" has meant failure to recognize many fractured carpal scaphoids in young adults and, in older people, the so-called sprain is all too often an impacted fracture of the lower end of the radius. The potential legal consequences of mistaking a fracture for a sprain are illustrated by the annual pleas of the Medical Defence Societies for routine X-ray examination of injured joints, and these pleas are peculiarly appropriate in connexion with the wrist. *If a wrist injury is severe enough to make the patient seek medical advice, it is severe enough to require an X-ray examination* and, to be adequate, the films must include antero-posterior, lateral and oblique views. If good X-ray films, exposed in these three planes, do not show any fracture, the provisional diagnosis of sprain or of contusion is permissible, but it should still be made with reserve. Should symptoms persist after ten or fourteen days, there should be no hesitation in repeating the X-ray examination, as the passage of one or two weeks may make a fracture line more obvious.

Severely sprained wrists are liable to be painful for a surprisingly long time, and this is particularly true of the injuries of the elderly. It is therefore no bad plan to treat such sprains by *splintage*, however normal the X-ray appearances. The best splint to use, even in old patients, is a light plaster cast, a "cock-up" plaster (fig. 7), and a short period of fixation in such a cast will give the damaged tissues their best chance of repair and will prevent many such sprains from becoming chronic. Naturally, prolonged fixation is not advised; two to three weeks should be ample, and a word of warning about the use of plaster of Paris in such injuries is necessary. Properly applied, there is no better splint, but the application is not easy.

To fashion a well-fitting and comfortable cast which holds the wrist and yet allows the essential freedom of finger movement demands experience. The dangers of undue tightness and of pressure on the thin skin covering the bony points of the elderly wrist are so real that one hesitates to recommend this line of treatment, for all its virtues, to any practitioner who has not had the necessary training in a plaster theatre. Greater safety is obtained by lightly padding and by splitting the cast and, as with all plasters and indeed all splints, a careful watch must be kept for undue tightness.

If the practitioner feels unable to treat such a wrist injury in plaster of Paris, a short aluminium cock-up splint is a good second-best. Care must again be taken that the fingers are not restricted in movement by the splint. Adhesive strapping is not well tolerated by elderly skin, and does not give nearly as much rest as does a splint or a plaster cast. If neither plaster nor splintage can be arranged, a firm bandage over a layer of wool is better than nothing, but only just.

The sprained wrist of the elderly patient is not a suitable injury for treatment by repeated novacain (procain) injections or for treatment with ethyl chloride sprays, however useful these measures may be in the strains of other joints in younger people.

FRACTURES OF THE LOWER END OF THE RADIUS

Diagnosis.—In adults, and especially in elderly adults, the most common wrist injury is the Colles's fracture, and the diagnosis of a severely displaced Colles's fracture does not usually present any difficulty. The striking

deformity (fig. 1) makes the lesion obvious. Difficulty arises, however, when there is no deformity. An impacted Colles's fracture with little or no displacement (fig. 2) is still commonly overlooked. In very old and frail patients the only

FIG. 1.—Colles's fracture. Clinical appearance of forearm and wrist viewed from the side: the "dinner-fork" deformity.

material sufferer from such an omission in the long run may be the practitioner's reputation, but in the more robust elderly person, minor degrees of displacement, which are not sufficient to produce visible deformity when the wrist is swollen immediately after the accident, may ultimately seriously impair wrist movement and may thus interfere with a hobby and cause annoyance in many ways. X-ray examination at the time of the injury will prevent recriminations later, as well as establishing the diagnosis and making the position of the fragments clear.

This plea for *X-ray examination* of injured wrists as a routine in al cases cannot be made too strongly or too often. It is not, however, a counse of clinical despair. No diagnosis should be made upon X-ray appearance alone, a rule to which wrist injuries are no exception. All wrist fracture have recognizable physical signs, and these physical signs must be sough

and the X-ray films interpreted in the light of them. The one constant physical sign of any fracture is tenderness. The tenderness is greatest at the site of the fracture and is therefore "bony" tenderness. Tenderness localized to a portion of a bone following the receipt of an injury is strong presumptive evidence of fracture. A "doubtful line" in an X-ray film should be read with this in mind. If the region corresponding to that line

be tender, the line indicates a fracture. If the tenderness lies elsewhere, then a suggestion that the line may be a vascular marking or some similar anomaly becomes more acceptable. The points of greatest tenderness in the more common wrist injuries are indicated in figure 3.
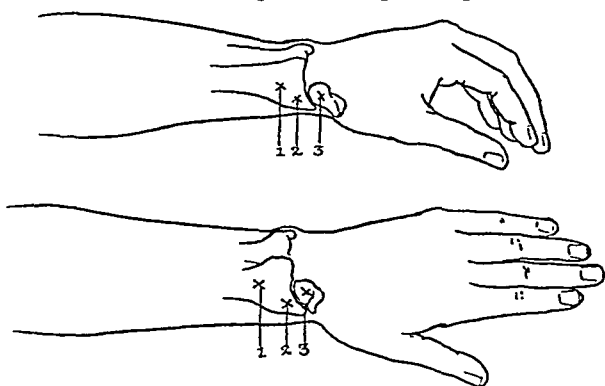
FIG. 3.—The positions of tenderness in common wrist injuries (1) in Colles's fractures: (2) in fractures of the radial styloid: (3) in fractures of the carpal scaphoid, recent or old.

Treatment.—An account of the methods of reduction and splintage of Colles's fractures is given in any standard textbook, and is outside the scope of this article. The practitioner who has to treat such fractures himself will, however, meet certain pitfalls about which help may be given.

Old bones break badly. Comminution is common, and the joint surface of the wrist is often broken up. Old joints stiffen all too readily even if their joint surfaces are intact; they stiffen permanently if their surfaces are shattered. Even if the joint surface is not involved, recovery from a Colles's fracture in an elderly person is apt to be slow, but it is not always realized how slow. At best, a severe Colles's fracture in an old person will require treatment and supervision for several months; at worst, the combination of old age and severe injury is liable to be followed by post-traumatic atrophy (Sudeck atrophy). This distressing syndrome, a combination of spontaneous pain with intractable stiffness and severe atrophy of the whole hand and forearm, is perhaps the worst fate which can befall an injured elderly limb.

All these misfortunes being the result of injury, it clearly follows that avoidance of further injury is of the greatest importance in treatment. The greatest danger of further injury lies in repeated attempts at reduction of fractures such as these. It can, indeed, be argued that a Colles's fracture with minimal displacement in a really old and frail patient should be recognized but not reduced, deformity being accepted as preferable to the infliction of further injury. Such a decision will be made rarely, and only in the presence of very real frailty, and it need hardly be added that the decision is one which should be confirmed by a second opinion, preferably

that of an experienced orthopædic surgeon. As a general rule, with few exceptions, Colles's fractures should always be reduced.

The *reduction* of any fracture at any age should be effected as gently as possible, and gentle reduction demands ideal circumstances. Adequate general anæsthesia (usually intravenous) should be used, and manipulation should be delayed, if necessary, until the patient is fit and prepared for this. Local infiltration and "whiffs of gas" are unreliable, and unreliable anæsthesia means rough reduction. Four persons are necessary for the manipulation: the manipulator, the anæsthetist, the person who will apply the plaster and someone who will control the arm above the elbow and apply the necessary counter-traction. No one person should undertake two of these tasks, for to do so will jeopardize the success of the manipulation; and the first manipulation should be the last.

Should the X-ray appearances after the first manipulation be deemed unsatisfactory, the advisability of a second attempt must be carefully considered. Usually, in any reasonably robust patient, a second attempt will be wise, especially if the remaining displacement be at all severe. A practitioner who has failed to reduce a Colles's fracture to his own satisfaction must, however, ask himself several questions before he makes a second

FIG. 4.—The open plaster of Paris cast used for Colles's fractures, (a) without, (b) and (c) with, the encircling gauze bandage. Note the close moulding, the freedom of the elbow and fingers, the soft bandage which retains the slab, and the position of *slight palmar flexion*.

attempt. Having failed once, will he succeed if he tries again? Will a second attempt, if successful, really contribute to the comfort and function of the patient's wrist, or will the trauma of a second manipulation do more harm than good? One thing is inexcusable, namely, the performance of a second manipulation on an elderly wrist merely to improve the X-ray appearances. As two attempts at reduction may well be dangerous, it goes without saying that three should never be made by the same operator. A second opinion is an advantage in any case of major wrist injury. This is essential in the event of a Colles's fracture which has defied two attempts at reduction.

After reduction and splintage, considerable swelling can still occur around a Colles's fracture. This must be anticipated. The use of an "open" or incomplete plaster cast is particularly recommended for this reason. The cast consists solely of a well-moulded slab (fig. 4) made of six thicknesses of plaster of Paris bandage, held in place by an ordinary gauze bandage, applied wet. Such a cast allows more "give" than does a complete one with encircling plaster bandages, and is far more easily released, if swelling is troublesome, by simple division of the gauze bandage along the front of the wrist and forearm. The plaster cast will, of course, allow full finger movement, and when insisting that the patient shall move the fingers fully and regularly the practitioner must not forget the shoulder. Wrist injuries are usually produced by a fall on the hand, in which violence is transmitted through the shoulder, which is at least "jarred". Old shoulders can stiffen very rapidly, and a stiff shoulder is an all too common result of a Colles's fracture. It can be prevented by ensuring that the patient, possibly assisted by a masseuse, shall put the shoulder through a full range of movement at least once daily during the period that the wrist is in plaster. It must be added that a stiff shoulder is invited by the prolonged use of a sling, which should be discarded the day after the plaster dries. A well-moulded plaster

cast is, at present, the only satisfactory splint for fractures of the lower end of the radius. Carr's splint is harmful, is useless even as a first-aid measure, and, with similar contrivances, has no place in modern fracture treatment.

FIG. 5.—Fracture of the base of the radial styloid, an unusual injury in the elderly. Commoner in young men. A "backfire" fracture.

FIG. 6.—Fracture of the tip of the radial styloid, a sprain fracture, due to the pull on the lateral ligament when the wrist is forced ulnar-wards.

FRACTURES OF THE RADIAL AND ULNAR STYLOID PROCESSES

The styloid process of the radius, fractures either through its base or through its tip. The fracture through the base (fig. 5) is not an injury of old people; the fracture through the tip (fig. 6) is. This latter is an avulsion fracture, the end of the process being detached by traction on the lateral ligament of the wrist when the hand is violently deviated towards the ulnar

side. These fractures do well. Displacement is trivial, and immobilization in a cock-up plaster (fig. 7) for three weeks is all that is needed.

FIG. 7.—Two views of the "cock-up" plaster. Note the very moderate degree of dorsiflexion of the wrist, and the freedom of the fingers and thumb.

Fracture of the tip of the ulnar styloid (fig. 8) gives a poorer outlook. This fracture is usually seen as part of the syndrome of a displaced Colles's fracture, the ulnar styloid tip being pulled off when the wrist and hand are forced over to the radial side. Detachment of the ulnar styloid, whether alone or as part of a Colles's fracture, is very prone to non-union, with persistent pain over the ulnar side of the wrist.

FIG. 8.—Fracture of the tip of the ulnar styloid, a common site for a painful non-union.

CARPAL INJURIES

Carpal injuries are not common after middle life. The scaphoid seldom fractures after the fortieth year, and the more severe injuries associated with dislocations of and around the semilunar are also seen at earlier ages.

FIG. 2.—X-ray print of impacted Colles's fracture without serious displacement; a fracture to be recognized by the localization of the

side. These fractures do well. Displacement is trivial, and immobilization in a cock-up plaster (fig. 7) for three weeks is all that is needed.

FIG. 7.—Two views of the "cock-up" plaster. Note the very moderate degree of dorsiflexion of the wrist, and the freedom of the fingers and thumb.

Fracture of the tip of the ulnar styloid (fig. 8) gives a poorer outlook. This fracture is usually seen as part of the syndrome of a displaced Colles's

fracture, the ulnar styloid tip being pulled off when the wrist and hand are forced over to the radial side. Detachment of the ulnar styloid, whether alone or as part of a Colles's fracture, is very prone to non-union, with persistent pain over the ulnar side of the wrist.

FIG. 8.—Fracture of the tip of the ulnar styloid, a common site for a painful non-union.

CARPAL INJURIES

Carpal injuries are not common after middle life. The scaphoid seldom fractures after the fortieth year, and the more severe injuries associated with dislocations of and around the semilunar are also seen at earlier ages.

It is, however, not uncommon for an old fracture of the scaphoid, inflicted many years before, to be brought to a practitioner's notice for the first time after a much later fall or "strain" of the wrist. Recent scaphoid fractures are quite often neglected by young patients (and by their doctors). When the immediate acute stage has passed, the young adult may accept his injured wrist as being "a bit weak" and may experience surprisingly little trouble so long as he avoids further injury or has not to attempt heavy work. Should a fall occur years later, however, the severity and duration of the symptoms then produced will be out of all proportion to the violence inflicted, and will usually lead to the discovery of the old fracture. The patient often requires a good deal of persuasion before he believes that it is in fact an old fracture, and the physical signs will be remarkably like those of a recent one, but the X-ray appearances will leave no doubt, as either a gap between the fragments or dense sclerosis on each side of the fracture will proclaim its age and irredeemable non-union (fig. 9 on plate).

Such a second injury to a previously damaged wrist is often followed by a rapid and progressive degeneration of the joint. These injuries must therefore be treated seriously, and a period of fixation in plaster of Paris advised. It should be needless to state that this fixation will not be designed to obtain union of the fracture (a long lost cause), but to give the wrist a few weeks of complete rest in the hope of minimizing and delaying its eventual breakdown.

THE COCK-UP POSITION

When the wrist is splinted or otherwise immobilized, it should be placed in the position of rest (fig. 10), which is the position in which the joint falls when the hand is allowed to lie relaxed, lying on its outer side. This is the so-called "cock-up" position, and is one of very moderate dorsiflexion. Any more severe degree of dorsiflexion is a position which imposes strain on the wrist, and forced dorsiflexion imposes enough strain to become painful in a matter of moments. It is a cardinal error to immobilize any joint in a position

FIG. 10.—The position of rest of the wrist. This degree of dorsiflexion must not be exceeded in "cock-up" splints or plasters.

of strain, and this is particularly true of elderly joints, and especially of the wrist. Cock-up splints which immobilize in extreme dorsiflexion will produce lasting stiffness. The one exception to the rule that the wrist should be immobilized in its position of rest is seen in the Colles's fracture, which should be splinted in *slight* forward flexion (fig. 4). It should be emphasized that an extreme forward position is even more crippling than the reverse. It should not be necessary to add that all wrist splints and plasters must leave the fingers full freedom, for of what avail is the most perfect wrist if its treatment has produced useless, stiffened fingers?

FIG. 9.—X-ray print of a very old fracture of a carpal scaphoid. The fracture only came to light years after it happened, being found after a second injury.

It is, however, not uncommon for an old fracture of the scaphoid, inflicted many years before, to be brought to a practitioner's notice for the first time after a much later fall or "strain" of the wrist. Recent scaphoid fractures are quite often neglected by young patients (and by their doctors). When the immediate acute stage has passed, the young adult may accept his injured wrist as being "a bit weak" and may experience surprisingly little trouble so long as he avoids further injury or has not to attempt heavy work. Should a fall occur years later, however, the severity and duration of the symptoms then produced will be out of all proportion to the violence inflicted, and will usually lead to the discovery of the old fracture. The patient often requires a good deal of persuasion before he believes that it is in fact an old fracture, and the physical signs will be remarkably like those of a recent one, but the X-ray appearances will leave no doubt, as either a gap between the fragments or dense sclerosis on each side of the fracture will proclaim its age and irredeemable non-union (fig. 9 on plate).

Such a second injury to a previously damaged wrist is often followed by a rapid and progressive degeneration of the joint. These injuries must therefore be treated seriously, and a period of fixation in plaster of Paris advised. It should be needless to state that this fixation will not be designed to obtain union of the fracture (a long lost cause), but to give the wrist a few weeks of complete rest in the hope of minimizing and delaying its eventual breakdown.

THE COCK-UP POSITION

When the wrist is splinted or otherwise immobilized, it should be placed in the position of rest (fig. 10), which is the position in which the joint falls when the hand is allowed to lie relaxed, lying on its outer side. This is the so-called "cock-up" position, and is one of very moderate dorsiflexion. Any

FIG. 10.—The position of rest of the wrist. This degree of dorsiflexion must not be exceeded in "cock-up" splints or plasters.

more severe degree of dorsiflexion is a position which imposes strain on the wrist, and forced dorsiflexion imposes enough strain to become painful in a matter of moments. It is a cardinal error to immobilize any joint in a position of strain, and this is particularly true of elderly joints, and especially of the wrist. Cock-up splints which immobilize in extreme dorsiflexion will produce lasting stiffness. The one exception to the rule that the wrist should be immobilized in its position of rest is seen in the Colles's fracture, which should be splinted in *slight* forward flexion (fig. 4). It should be emphasized that an extreme forward position is even more crippling than the reverse. It should not be necessary to add that all wrist splints and plasters must leave the fingers full freedom, for of what avail is the most perfect wrist if its treatment has produced useless, stiffened fingers?

THE TREATMENT OF CARCINOMATOUS ULCERS

By DUNCAN C. L. FITZWILLIAMS, C.M.G., M.D., Ch.M., F.R.C.S.

Consulting Surgeon, St. Mary's Hospital; Surgeon, Mount Vernon Hospital.

MASSES of carcinomatous tissue, whether they be primary or secondary growths, often break down and ulcerate. When that happens there is trouble and misery for the patient, and this in turn upsets friends and relations and so is reflected on to the practitioner. Ulceration of cancerous masses in connexion with the breast is perhaps the type most frequently seen and the one which gives rise to most trouble.

The ulcers which form vary between two extremes, although every gradation between the two is met with. They may be either shallow depressed areas, as in the atrophic cancers, with smooth fibrous bases, as if all the granulation tissue had been scraped away, and with hard rolled-over edges; or they may be of the fungating type, in which large, soft, moist cauliflower-like masses of tissue protrude from the surface of the wound: this tissue bleeds easily and constantly oozes fluid.

Either lesion requires constant attention, and frequent dressings which always remind the patient of her disability. The second form is of course much the worst of the two. These ulcers are often accompanied by chronic pain, a good deal of which is imaginary and caused by the constant worry, continual feeling of ill health, the ever present odour, and want of sleep which the wretched patient must always endure. Practically, too, these ulcers are a great drain on the strength of the patient owing to the continuous discharge and absorption from their surfaces; whilst psychologically they have a most depressing effect upon the patient, and are a cause of annoyance, to say the least of it, to their friends. There are few conditions which a practitioner likes less. Any advice therefore that can be given to help in the treatment of such cases should be welcome.

LOCAL APPLICATIONS

It will be most people's experience that local treatment by the old-fashioned ointments has little effect; sulphonamide ointments are little better. Many other substances have been tried, such as liquid fluorescene, tanning with tannic acid, which merely dries the lesion for the time and causes more pain; the actual cautery which can remove redundant tissue and lessen discharge, but that is all. The smell can be slightly lessened by the use of powdered charcoal, but this is black and gets over everything. Paraffin seems the best dressing, but is not improved by combining with picric acid, which has the disadvantage that gloves must be worn or the fingers will be stained yellow.

RADIUM THERAPY

My experience has taught me that there is only one form of treatment which

is of any value, and by value I mean that it will heal the ulcer whatever its form, free the patient from pain and anxiety, and really improve her general health. If it happens to convey to her mind the false impression that a cure is taking place, then quite frankly so much the better. The one really efficient remedy is radium. Its effect is little short of miraculous and must be seen to be believed. It would be stupid to assert that every ulcer can be completely healed by radium or any other method, but it can be safely said that every case will improve in a most remarkable way under its use.

The application of radium varies with the site, shape, and size of the ulcer. No attempt need be made to clean or render aseptic the surface of the ulcer; that is now recognized as unnecessary. An anæsthetic should be given, but this need be only a short one, if everything is prepared beforehand. This is sometimes important in old people whose general health is undermined.

Dosage.—The amount of radium to be used varies, according to the length of needle, from 0.5 mgm. in a needle of 20 mm. in length to 3 mgm. in one of 65 mm. in length. The screenage varies too, from 0.5 mm. of platinum in the lower grades to 0.6 in the higher grades. The method of mounting the needles and fixing them in place need not be discussed here.

Technique.—In the case of *the flat depressed ulcer* of the more chronic forms of cancer, the needles are inserted about a quarter of an inch outside the rolled-over edge of the ulcer, and should be long enough to underlie the edge of the opposite side. In large ulcers the needles may not be long enough to stretch across, in which case they are put in from the two sides and overlap in the centre. The needles should be placed about a quarter of an inch apart and should cover the entire area. Care must be taken that they do not penetrate the floor of the ulcer or bleeding will take place; such bleeding can usually be avoided altogether. In these cases the needles are best inserted alternately on both sides of the sore. The threads on which they are mounted can then be tied across the ulcer and thus serve to keep the needles in place while they are being worn.

With *the fleshy, prominent, cauliflower-like mass,* a different method is used. The base of the sore is treated in the same way, but shorter needles are inserted into the soft tissue of the mass itself. These will probably work loose and the ends of the threads must be fixed to the skin with strapping. In those rare cases which are sometimes still seen in which there are definite pockets in the prominent tissue, tubes can be inserted containing up to . 30 and even 50 mgm. of radium. These are mounted on thin copper wire, the ends of which are fixed to the skin with strapping; if the wire is twisted (gauge 25) it is stiff enough to prevent the tube moving. These tubes should not be left in one place for more than forty-eight hours. They can be moved daily when the wound is dressed. Heavy dosage is called for as necrosis of the cancerous tissue is desired, and this is quite a different thing from causing necrosis of healthy tissue, which takes months to heal.

Gauze dipped in paraffin is used to dress the area; the moisture is best

conserved by covering it with a layer of green protective or jaconette, it will not then stick to the surface, and can be removed without pain. The radium is left in place for *about* a week; experience alone will dictate the time. Considerable improvement may be seen at once when the needles are removed, but improvement will continue for at least two months.

Signs of healing.—In the flat ulcers the rolled-over edge will first disappear, the floor will look more healthy and the skin at the edge will begin to grow in. The area of the ulcer shrinks almost at once. The prominent masses protruding from the surface will begin to shrivel and get smaller, eventually coming down to skin level, by which time the skin edges will have begun to grow in. The small ulcers will heal at once, often within fourteen days. The larger ones will take longer, and the very large ones may need another application of radium before they heal completely.

If the effect of the radium is striking on the ulcer itself, the effect of the treatment on the patient is equally remarkable. She sees for herself the condition improving, the ulcer growing smaller, whereas formerly the only change was an increase in its size. The dressings become less frequent; the horrible odour disappears. The evidence of improvement is patent to all. She imagines that a cure is being brought about. She only too willingly disregards its limitations, and hope is again born in her mind. As she becomes more comfortable and happy, her health improves, her appetite returns and she may even gain in weight; in fact her whole mental outlook changes.

ILLUSTRATIVE CASES

The following cases have been chosen to illustrate these points.

Miss S. Aged seventy-two. Seen 4.4.27.
History: Had a lump in her right breast for over two years; for this she had herbal treatment—medicine and ointment. She then went to another herbalist and had slippery elm poultices and sweet oil. This brought out a purple-red patch which ulcerated, and the herbalist said "it would get larger before it got better".
Examination: The breast had shrunk; at its outer side was an ulcerating area, 3 in. by 3 in., over a hard tumour which was attached to the muscles; there were hard glands in the axilla.
Interstitial radium was applied, about 12,000 mgm. hours being given with excellent results. The ulcer healed rapidly but the skin over the scar was scaly. The growth became hard and the glands which were treated by radium at the same time shrunk to nothing. Her family practitioner wrote to me eight years later that she had died of secondaries in the liver and that secondary nodules appeared on the left side of her chest. The old condition never showed any signs of activity.

Mrs. C.S. Aged fifty-six. Seen 15.8.31.
History: Known of a lump for a year.
Examination: There was an elongated lump stretching from the left nipple to the axilla, as if one lobule of the breast was effected. This was attached to the skin and had ulcerated through at one place, the ulcer being the size of a shilling. She had glands in the axilla and above the clavicle. Quite inoperable.
17.8.31. Surface radiation. 12,320 mgm. hours to breast; 10,240 to the axilla and 10,080 above the clavicle.
10.10.31. Readmitted to Mount Vernon Hospital. The ulcer had completely healed. She had 10,080 mgm. hours to the breast, 10,880 to the axilla, and 8 160 above the clavicle.

21.8.33. Patient readmitted. She still had a mass attached to the skin and small shotty glands in the axilla. The mass was removed and the axilla cleared.

Pathological report: Spheroidal-celled carcinoma in breast and glands.

4.2.37. Metastases in the spine. She died later in that year.

We did not attempt to give her a large enough dose to destroy all the cancer in her breast, as it was thought that with the existing glands above her clavicle the internal metastases which would later develop would carry her off whatever we did. Her ulcer was healed and never needed any more dressing.

Mrs. H. Aged fifty-eight. Seen 30.11.32.

History : Mr. Sampson Handley removed her breast in 1925. She then had deep X-rays and had radium in her axilla, but the wound had never healed.

Examination: She was not looking well, was breathless and had a slight vagal cough. Over her old scar was an ulcer 4 in. by 3 in., which had discharged and had needed constant dressing for seven years. Secondary nodules were appearing round about. The edges of the ulcer were hard and prominent, the surface was bare.

Radium was applied and she went home. I did not see her for nearly a year. The ulcer by that time was soundly healed and had required no dressing for some months. She was going down hill. She died 8.8.33 after repeated tappings.

Mrs. G.M. Aged forty-seven. Seen 30.6.34.

History: She had had her breast removed in 1927; since then she had had two more operations, one for obstructed Meckel's diverticulum, and the other for piles.

Examination: She had a secondary mass on her chest, to this radium was applied in St. Mary's Hospital and it disappeared.

In September, 1941, she was readmitted with another recurrence. She now had an ulcer which had been getting worse for six months but she did not come for treatment. It was 3 in. by 3 in. She was given 6,360 mgm. hours. The ulcer healed completely. In October, 1942 she came again. The ulcer had broken down. More radium was given and it healed. She was last seen in 1945 with the ulcer completely healed.

Miss B. Aged sixty-three. Seen 4.10.39.

History: Two years ago had a small lump removed from her left breast which had been there for a year. She was told "no pathological report was needed". A year later something came again but this time she did nothing until an ulcer had developed and got steadily larger.

Examination: Now there is an ulcer over the upper part of the left chest 3 in. by 3 in., the edges of which are hard and raised. She has been dressing it for a year.

5.10.39. Interstitial radium applied and tubes put on the surface. By January the ulcer was healing nicely, the discharge was no longer offensive. The improvement in her general health is remarkable. In March the ulcer had dried up. She remained fairly well until internal metastases developed and she died in January 1941.

The next case was perhaps the most spectacular.

Mrs. A.B. Seen 1.5.39.

History: She had known of a lump in her right breast for eight months.

Examination: There is a large raw triangular mass protruding through the skin, which is raised about an inch above the surface; it discharges freely. Under this is felt a mass attached to the deep fascia. There is a mass of glands in the axilla.

5.5.39. Interstitial radium applied and again twelve days later. The growth receded and the area healed completely.

19.4.40. Surface radiation applied to the underlying mass.

3.6.41. The skin is sound; the mass has fibrosed and is quite stationary; the glands in the axilla are fibrosed.

21.9.42. The patient died of internal metastases. From the time she was first seen the condition was too advanced for operation to be of any use.

I can only hope that these cases will encourage others to treat all forms of carcinomatous ulcers in a like manner.

THE PROPHYLACTIC USE OF THE SULPHONAMIDES IN INFECTIVE DISEASES

By JOHN BOYCOTT, D.M.

Lately Assistant Bacteriologist, St. George's Hospital.

ALTHOUGH the control of infective disease in its broadest aspects must remain the concern of the Public Health authorities, the practitioner is more or less often faced with the problem of prophylaxis of infection within the family or some small community, such as a school. In this article it is proposed to deal with one aspect of this problem, namely, the use of the sulphonamides.

MENINGOCOCCAL INFECTION

Several reports have appeared of the successful termination of an epidemic of meningococcal infection in a closed community by mass dosage of all personnel with a relatively small dose of sulphadiazine (Kuhns *et al.*, 1943). Personal experience in a troopship containing West African troops (who are highly susceptible to meningococcal infection) has confirmed this. Nevertheless, sporadic cases of such infection without epidemic spread are common enough and it is difficult to submit this method of prophylaxis to a controlled trial. It appears to have no serious disadvantage in a closed community, but the risks of producing a "drug-fast" strain of the organism are too great to justify its use among the general public in the face of an epidemic.

GONORRHŒA

In a trial in the United States (Loveless and Denton, 1943) it was found that the administration of 6 gm. sulphathiazole to every man returning to camp, irrespective of whether he admitted to sexual intercourse or not, was followed by a dramatic fall in the incidence of gonorrhœa to one-tenth of the previous figure. What is more difficult to explain is that at the same time there was a less impressive decrease in the number of fresh cases of syphilis.

RHEUMATIC FEVER

No claim is made that the fresh case of rheumatic fever can be prevented. Relapses, on the other hand, are so frequently associated with a hæmolytic streptococcal infection of the upper respiratory tract that it seemed justifi-

able to try the effect of treatment with small doses of sulphanilamide over long periods, since the hæmolytic streptococcus is particularly susceptible to this drug. The results of six tests (Barclay and King-Lewis, 1945) are tabulated below:—

TABLE I

Test No.	Age (yrs)	Duration of test (yrs)	Daily doage (grammes)	Controls		Treated	
				No.	relapses	No.	relapses
(1)	6–16	2	0.6–1.5	41	5	41	1
(2)	under 13	1–2	2–3	146	31	188	1
(3)	3–16	3	1–3	46	21	78	2
(4)	3–13	1–2	1.5–2	14	4	7	1
(5)	7–37	4	1–1.3	150	15	79	0
(6)	6–15	1–2	1–2	108	23	108	1

In every case but one toxic reactions were regarded as negligible. In test no. 4 the patients were ambulant and it was found impossible to control the amount taken; one child died from agranulocytosis. It is probable that one of the newer compounds, sulphadiazine or sulphamezathine, would be preferable, but these were not available when these trials were made.

UPPER RESPIRATORY TRACT INFECTIONS

Two experiments designed to test the efficacy of a daily dose of a sulphonamide drug in the prophylaxis of infections of the upper respiratory tract are of interest for their divergent but not incompatible findings.

To meet the exceptionally high incidence of such infections among naval recruits under training it was decided to give a daily dose of 1 gm. of sulphadiazine to approximately 250,000 men, leaving an equal number as controls (Coburn, 1945). Recruits are notoriously subject to epidemic infections; a fact reasonably ascribed to overcrowding, a high rate of change in the make-up of the community and the continual introduction of susceptible new entries Within a few weeks of the institution of the treatment the effects were seen in a reduction of the hospital admissions among the treated groups for respiratory tract infections by 80 to 90 per cent. and for streptococcal infections by 85 per cent. Meningococcal infection was to all intents abolished. For every case of rheumatic fever among the treated recruits fourteen occurred in the controls. Success in the prophylaxis of pneumonia was less marked; streptococcal pneumonia became rare but pneumococcal infections were not reduced to the same low level. No effect was seen among the viral infections, colds, influenza, measles, but secondary bacterial infection was much reduced with a consequent lowering of the period of incapacity. Mild reactions occurred in about 0.5 per cent. of cases, nearly all of which were skin rashes. Renal complications were not seen. There was no

evidence that prolonged ingestion of the drug induced sensitivity; those w¹ were sensitive showed symptoms when first treated or not at all.

These were observations of the first importance, promising a startlin reduction in the risk, not only of minor upper respiratory tract ʿ ɪfʾ ʾ but also of their more serious sequelæ, and apparently applicable to tʰ population at large. Some evidence had arisen that the risk of producing ʌ occasional drug-fast strain was a real one but that the danger to be ; ˉ was slight. A report published six months later makes it clear that opʿ ʿ on this score was unfounded and that, in fact, serious results might ' expected as a direct consequence of the prophylactic use of small daily doˢᵉ of sulphadiazine (Young et al., 1945). The observations were made at one the naval training stations involved in the original trial. So successful hʌʾ this appeared to be that the daily administration of 1 gm. of sulphaʿ ʿ ʌɪ had been extended to all personnel. Within a short time a considerable increase in the number of streptococcal infections was noticed and attributed to an increased incidence in the general population. Examination of the strains of streptococci responsible showed, however, that one type (type 19), previously responsible for 28 per cent. of infections, was now implicated in 95 per cent. This and two other prevalent types were now drug-fast. It is probably no more than accidental that these types were all highly communicable and responsible for numerous cases of scarlet fever, but this served to underline the dangers involved.

A more detailed experiment on a smaller scale was made in a home for defective children, where infections of the upper respiratory tract had been more than usually common in the previous winter (Siegel, 1943, 1944, 1945). No difference between treated and untreated groups could be found in the occurrence of these ailments except that secondary infections (and consequent duration of stay in bed) were less in the treated group. However, it is fair to say that the total incidence in both groups was far less than in the previous winter. The chief interest of this trial lay in the detailed examination of the flora of the throats of the subjects. Without going into details it may be said that drug-fast strains of several organisms were produced which spread rapidly through the community without, in this instance, serious consequences.

These two experiences are convincing evidence of the danger to the individual and to the community involved in the prophylactic use of the sulphonamide drugs over a long period. Whether drug-fast strains of pathogenic organisms will become common as a result of the general use of these compounds in practice it is impossible to say; certainly no convincing evidence of this is yet available. Nevertheless, it was suggested with reason that the poor results obtained in the treatment of gonorrhœa among army personnel in Italy were due to the local prevalence of strains of the gonococcus which had been rendered drug-fast by the widespread and uncontrolled use of sulphonamide drugs by the civil population (Campbell, 1944).

CONCLUSION

Are there circumstances that justify the prophylactic administration of sulphonamide drugs? The danger appears to lie in the production of the drug-fast strain of the pathogenic organism alone; under medical supervision the risks of intoxication are slight.

In penicillin another drug is available, effective in most cases against the same organisms that are sensitive to the sulphonamide drugs, on which to fall back if a sulphonamide-fast strain is produced. Induced resistance to the sulphonamide drugs does not influence the susceptibility of an organism to penicillin.

As a personal opinion I believe that the prophylactic use of the sulphonamide drugs is justified in the following circumstances:—

(1) The convalescent case of rheumatic fever under institutional supervision.

(2) The school or similar community threatened with an epidemic of meningococcal or streptococcal infection.

(3) The small group living a regulated life, among whom it is of the greatest importance to avoid minor illnesses; e.g., an athletic team in training.

With the exception of cases in (1), treatment should never be continued beyond a period of a few weeks. A daily dose of 1 gm. of sulphadiazine, taken at night, should provide adequate protection, irrespective of age or background.

References

Barclay, P. E., and King-Lewis, F. L. (1945): *Lancet*, ii, 751.
Campbell, D. J. (1944): *Brit. med. J.*, ii, 44.
Coburn, A. F. (1945): *Bull. N.Y. Acad. Med.*, **21**, 281.
Kuhns, D. M., Nelson, C. T., Feldman, H. A., and Kuhn, L. R. (1943): *J. Amer. med. Ass.*, **123**, 335.
Loveless, J. A., and Denton, W. (1943): *Ibid.*, **121**, 827.
Siegel, M. (1943): *Amer. J. Dis. Child.*, **66**, 114.
—— (1944): *Ibid.*, **67**, 363.
—— (1945): *Ibid.*, **70**, 89.
Young, D. C., et al. (1945): *J. Amer. med. Ass.*, **129**, 921.

THE EARLY RECOGNITION OF DISEASE
XII.—DISEASES OF THE BLOOD

By JOHN F. WILKINSON, M.D., M.Sc., Ph.D., F.R.C.P., F.R.I.C.

Physician in Charge and Director of the Department of Clinical Investigations and Research, Royal Infirmary and University of Manchester.

THE early diagnosis of blood diseases may often present difficulties, particularly when the characteristic blood picture has not developed sufficiently, or if it has been obscured by previous non-specific treatment with liver, iron and vitamins. It is thus of prime importance that antianæmic treatment should not be given until a diagnosis has been made.

Once the signs and symptoms of any particular blood disease have developed, a correct diagnosis is readily made, but it is in the earlier stages that difficulties arise, when perhaps only one or two of the symptoms have become manifest. It is also at this stage that confusion may arise owing to the often vague and ill-defined nature of the early symptoms, which may suggest disturbances of other systems.

EARLY SYMPTOMS

On careful inquiry into the modes of onset of diseases of the blood, it becomes clear that, often for years previously, there has been perhaps only a single symptom, such as increasing tiredness or lack of energy, inability to carry on a day's work as easily as before, vague and frequently irregularly occurring symptoms referable to the gastro-intestinal system, such as sore tongue and mouth, indigestion, heartburn, flatulence, distension of the abdomen after meals, intermittent diarrhœa, and the like, whilst other patients may only complain of increasing pallor, difficulty in swallowing solid food, brittle and deformed nails, hæmorrhages (e.g. hæmatemesis, melæna, purpura, menorrhagia, bleeding gums), or early changes in the nervous system in the form of neuritis or paræsthesiæ. Marked loss of weight and gross anæmia are not as a rule early signs, although the latter may appear as the first sign in certain acute conditions—in fact, there is often little or no anæmia in the early stages.

It is clear that the early symptoms may be extremely ill-defined and varied in character, extent and severity, differing widely in different patients according to age, sex, causative factor, rapidity of onset and severity of the blood changes. In some patients blood changes may be late in disclosing their typical characteristics, whereas in others pallor with anæmia may be the first thing to attract attention. Occasionally the first complaint has been associated with the discovery of an enlarged spleen. It therefore becomes necessary to consider the implications and investigation of patients complaining of mild symptoms such as these.

DIAGNOSTIC PROCEDURES

I have previously considered in some detail the diagnosis of fully developed anæmias from a careful history of the condition and clinical examination with the necessary investigational procedures, which must include as a minimum a full blood examination, investigation of the bone marrow taken by sternal puncture, and a fractional analysis of the gastric contents (Wilkinson, 1945).

The *blood examination* must include an estimation of the red and white blood cells, hæmoglobin, a differential white cell count, reticulocytes, platelets, red cell volume and fragilities, and, as required, the van den Bergh reaction and Schumm's test. In special cases other investigations may be required, but the details need not be discussed here.

Recent work has demonstrated the simplicity and extreme value of the *sternal marrow biopsy*, especially in difficult or early diseases of the blood, but considerable experience is necessary for a correct interpretation of the smears so prepared. In the early stages it is often difficult or even impossible without sternal puncture to diagnose with certainty an early acute leukæmia when the white cell count is low, for clinically and in the blood count it may simulate pernicious anæmia or, if there is a severe anæmia, an aplastic anæmia; sometimes in the presence of hæmorrhagic manifestations a purpura may be suspected; a sternal biopsy will usually reveal the true condition often weeks before the peripheral blood reflects the true diagnosis. Similarly, the differentiation of megalocytic anæmias, such as pernicious anæmia or achrestic anæmia with megaloblastic hyperplasia, from early hæmorrhagic anæmias with marked normoblastic hyperplasia, or acute leukæmia, is rendered easy by this technique.

The discovery of an aplastic or hypoplastic marrow at once differentiates such an anæmia from the leucopenic or thrombocytopenic conditions found in agranulocytosis and thrombocytopenic purpura respectively. Recently we have been able to demonstrate the value of this technique in the diagnosis of two cases of Gaucher's disease by the finding of Gaucher cells in the biopsy smears.

Fractional gastric analysis is an important diagnostic procedure, since it is now universally accepted that in pernicious anæmia and subacute combined degeneration of the spinal cord, achylia gastrica is always found without exception and, since this appears to be of life-long standing in the patient, the finding of free hydrochloric acid in the stomach of a patient suspected of having either of these conditions excludes such diagnosis at once and, further, practically excludes the future possibility of such diagnosis in that patient.

The occurrence of an anæmia, resembling either the megalocytic or microcytic type, in association with gastric carcinoma can usually be differentiated, since the fractional gastric analysis in these cases will show an achlorhydria or hypochlorhydria with abnormally high total acidity titres,

and the presence of lactic acid, blood, mucus and sometimes pathological cells in the gastric contents.

CLASSIFICATION

The main blood diseases I propose to consider here fall into these groups:—

Anæmias (a) Secondary to hæmorrhage, whether acute or chronic, intermittent or continuous.

(b) Aplastic anæmia, or hypoplastic anæmias, as following severe infection or sepsis.

(c) Hæmolytic anæmias.

(d) Megalocytic hyperchromic anæmias.

(e) Microcytic hypochromic anæmias.

Polycythæmia.

Leukæmias.

Neutropenias.

Hæmorrhagic and purpuric conditions.

Splenomegalic diseases (a) Banti's syndrome (splenic anæmia).

(b) Lipoidoses, e.g. Gaucher's disease, Neimann-Pick's disease and Hans-Schüller-Christian disease.

ANÆMIA DUE TO BLOOD LOSS

This condition does not lead to any difficulty in diagnosis, since it is always a sequel to an acute or chronic hæmorrhage from the alimentary or genito-urinary tracts, or following injury, or as a secondary feature to other diseases of the blood or vessels, such as hæmophilia, purpura, telangiectasia, and the like. The cause is obvious and no difficulty arises, but it may often happen that a very slight constant occult hæmorrhage may be unobserved for years and lead to the insidious onset of a secondary anæmia such as may occur in chronic peptic ulcer.

These patients complain of loss of energy, weakness, sometimes shortness of breath, palpitation and loss of weight; they show as main features a reduction in the hæmoglobin and red cell counts with, as a rule, a low colour index and sometimes a slight leucocytosis. There are no diagnostic features in the blood, sternal marrow or gastric secretion.

APLASTIC OR HYPOPLASTIC ANÆMIAS

In anæmias due to aplasia or hypoplasia of the bone marrow, the patient shows a pale waxy colour of the skin, pallor of the mucous membranes, marked weakness, debility and dyspnœa, disinclination to do anything, loss of weight and, in the later stages, recurrent epistaxis and bleeding gums.

These primary conditions begin very insidiously between the ages of fifteen and forty years with general tiredness, lack of energy, an increasing degree of pallor of the skin and dyspnœa on exertion, and there may be some bleeding of the gums in the early stages, especially if any teeth have been

extracted, which may lead the patient to date his illness from such incident. The secondary types may appear at any age after exposure to toxic agents, such as benzene or radio-active substances, or as a sequel to severe and overwhelming infection or sepsis.

In the early stages there may be only a mild normocytic anæmia, but this rapidly progresses to a severe degree with neither evidence of red cell degeneration nor hæmolysis; the reticulocytes are not increased in numbers, the van den Bergh reaction and Schumm's test are negative, the gastric acidity is normal, and the spleen is not enlarged. There is no response to treatment.

THE HÆMOLYTIC ANÆMIAS

The hæmolytic anæmias include a number of well-recognized diseases with a few less well-defined chronic ones. Among the former are acholuric jaundice, acute hæmolytic anæmia of Lederer, hæmolytic (spherocytic) anæmia, and erythroblastosis fœtalis.

The common features in this group are increasing weakness, lack of energy, palpitation, dyspnœa, jaundice and loss of weight with severe hæmolytic processes associated with a megalocytic or normocytic anæmia, polychromasia, high proportions of normoblasts, and reticulocytes in the peripheral blood, increased red cell volume, positive van den Bergh reaction and Schumm's test, normal gastric acidity, marked normoblastic hyperplasia of the bone marrow, and usually a moderate splenomegaly. In the early stages there may be only mild jaundice and some anæmia, whilst in acholuric jaundice the abnormal red cell fragilities are variable and may be noted early or later.

THE MEGALOCYTIC ANÆMIAS

In the megalocytic anæmias it should be remembered that a fault at any stage of the gastro-hæmopoietic mechanism (Wilkinson, 1936) will lead to the same blood and marrow pictures, but other features may differ, thus indicating different forms and modifications of treatment. The chief representative in this group is pernicious anæmia which, when fully developed, and usually over the age of forty-five years, is as a rule characterized by dyspnœa, palpitation, a lemon-yellow colour, prematurely grey hair which is soft and silky, glossitis and ulceration of the mouth, flatulent dyspepsia, diarrhœa or constipation, paræsthesiæ in the limbs, or more marked signs and symptoms of postero-lateral involvement of the spinal cord, and occasionally optic atrophy. The findings show variable spleno-megaly, usually slight, occasionally retinal hæmorrhages, severe megalocytic anæmia (with high colour index), polychromasia, aniso- and poikilo-cytosis, reticulocytosis for about two weeks after active treatment or spontaneous remissions, invariable achylia gastrica and a typical megaloblastic hyperplasia of the bone marrow. In the early stages there may be only slight anæmia, soreness of the tongue and mouth, flatulent dyspepsia, or a long history of recurrent diarrhœa which may have led to a previous investigation of the gastric condition—disclosing an achylia gastrica, which is probably

hereditary—long before there are any blood changes. It is very common to find in other members of the family a history of pernicious anæmia, hypochromic anæmia, postero-lateral sclerosis, or achylia gastrica with gastro-intestinal symptoms.

Similar symptoms may be noted in *achrestic anæmia*, which comes on between the age of twenty to fifty years and closely resembles pernicious anæmia clinically, but in this condition there is a normal gastric secretion, never any neurological signs or symptoms, and poor or little response to treatment.

In megalocytic or "hæmolytic" *anæmia of pregnancy*, there should be no difficulty at all in diagnosis, since a megalocytic anæmia occurring during pregnancy or the puerperium is found without an achlorhydria, which responds to treatment, clearing up completely after the puerperium.

HYPOCHROMIC MICROCYTIC ANÆMIA

Hypochromic microcytic anæmia, occurring almost exclusively in women between twenty and fifty years of age, is usually insidious and chronic in its onset, so that the patient is not aware of its development until she begins to notice that she is unable to do her work and feels tired, weary and generally unfit. With it may develop a flatulent dyspepsia, some diarrhœa, angular stomatitis (probably also associated with deficiencies of vitamin B constituents), soreness of the mouth and tongue, with or without recurrent ulceration, dry, coarse, brittle hair, koilonychia (a pathognomonic sign), menstrual disturbances, loss of weight, whilst in the Plummer-Vinson syndrome, dysphagia is also a pathognomonic feature. Examination shows pallor of the mucous membranes and skin with a slowly progressive anæmia but rarely any splenomegaly. Blood examination discloses a variable hypo-chromic microcytic anæmia, with often a very low colour index, especially in the later stages; there is no evidence of hæmolysis; fractional gastric analysis most frequently shows achylia gastrica, and the bone marrow is normoblastic in type. The van den Bergh reaction and Schumm's test are negative. There is a rapid response to iron therapy with ascorbic acid and a hydrochloric acid and pepsin mixture. It is now recognized that a megalocytic or microcytic anæmia may develop gradually in certain patients after a gastro-enterostomy or gastrectomy and is manifested in the first place by loss of energy, tiredness, increasing pallor and anæmia, and maybe loss of weight; glossitis and ulceration of the mouth may be troublesome symptoms.

POLYCYTHÆMIA

In polycythæmia the first symptoms and signs appear as a rule after the age of forty-five and may be in the form of severe headaches or a very painful erythromelalgia in the lower limbs which, with some degree of scleroderma, may suggest an early Raynaud phenomenon. With the development of the dark red appearance of the skin, especially of the face, and the maroon colour of the mucous membranes of the mouth, lips and tongue, and the variable

degree of splenomegaly, the diagnosis becomes obvious. This is confirmed by the blood count which shows a much increased red blood cell count (7–14 × 10⁶ per c.mm.) and hæmoglobin (up to 140 per cent. or more) with some leucocytosis. The van den Bergh reaction and Schumm's test are negative, and fractional gastric analysis usually shows an achlorhydria gastrica, but occasionally a high acidity may be noted and associated with symptoms and signs of duodenal ulcer (I have seen two such cases). The sternal marrow shows a normoblastic reaction but red cell packing is notable.

THE LEUKÆMIAS

The leukæmias may be acute or chronic in type. *Chronic myeloid and lymphatic leukæmias* should offer no difficulty in diagnosis. Usually beginning in middle or later life, their onset is very insidious and progress is usually slow in the early stage. The first symptoms are nearly always loss of energy, undue fatigue, shortness of breath and then loss of weight, but I have seen cases in which, for example, the first sign of a lymphatic leukæmia was an enlarged tonsil or a small lump in the skin. The patient looks sallow or develops a greyish pallor. Enlargement of the spleen takes place, progressing steadily until the whole abdomen is greatly distended; it may be almost completely filled with that organ, thus further embarrassing the diaphragmatic movements and causing mechanical pressure on the abdominal vessels. It is common to find marked enlargement in the chronic types, whilst hepatic enlargement may also occur in chronic myeloid leukæmia.

Examination of the blood usually shows a much increased total white cell count (200,000–500,000 per c.mm., occasionally more) with increase in the myeloid or lymphoid series according to the type—myeloblasts, myelocytes and premyelocytes in the former, and lymphoblasts in the latter condition.

More difficulty arises in the diagnosis of *the acute leukæmias*. These begin in an insidious manner without warning or known cause. They are most commonly seen in young adults and children of all ages. The first signs are lack of energy, a disinclination to do anything or to play, a waxy, marble-like pallor of the skin; and then follows a steadily increasing and severe anæmia with or without some bleeding of gums or epistaxis. Usually there is little or no enlargement of the spleen and the glands are rarely affected. It is at this stage that the blood count may be difficult to interpret, showing a severe anæmia with red blood cells about 1.0 × 10⁶ to 2.5 × 10⁶ per c.mm. or so, and hæmoglobin 20–60 per cent., whilst the total white cell count is usually between 1000 to 7000 per c.mm. The differential white cell count may be quite unhelpful and non-specific or may show a few abnormal primitive white cells. It is at this stage that an incorrect diagnosis is often made owing to the superficial resemblance to an aplastic anæmia or pernicious anæmia. However, a careful review of the history, the young age of the patient, mode of onset and general clinical appearance and

colour should serve as a warning; a sternal marrow biopsy will invariably indicate the leukæmic nature of the condition, which in the course of a few days or weeks runs to a fatal termination, before which, however, the peripheral blood will show more typical features of an acute leukæmia.

A relatively rare condition, *acute monocytic leukæmia*, is seen from time to time—its onset is quite characteristic. In most cases it starts insidiously with some lack of energy and general fatigue; then a peculiar maroon coloured œdematous swelling of the gums resembling scurvy is noted with fetor of the breath: this frequently appears to follow tooth extraction and may be associated by the patient with the oral condition, the true nature of the disease not being at first recognized. The condition progresses rapidly, the gums continuing to swell so that the teeth are completely covered with the mass of bluish or maroon coloured swollen gum which does not respond to any local or general treatment. The spleen and lymph glands are not enlarged but examination of the blood shows a slowly rising total white cell count and a rapidly increasing number of monocytes and monoblasts, so that the differential white cell count shows ultimately 90 per cent. or more of these latter with a total count of 40,000 to 100,000 per c.mm. There is a variable degree of anæmia. The condition is rapidly fatal in a few weeks. No other condition shows this characteristic onset, progress and blood picture. The sternal marrow shows a picture closely resembling the peripheral blood smear.

AGRANULOCYTOSIS

Owing to its etiology, agranulocytosis, or malignant neutropenia, may present some difficulties in the early stages of its onset. As a rule it is a result of exposure to some toxic agent, such as the sulphonamide derivatives, barbiturates, amidopyrine, preparations of gold, arsenic, bismuth, benzene, thiouracil, and many other similar therapeutic drugs.

The first symptoms are usually pyrexia, then soreness and necrotic ulceration of the mucous membranes of the throat, mouth and fauces, followed by brawny swelling of the neck. Sometimes the necrotic ulceration appears first or solely in the mucous membranes of the rectum or vagina. There is no evidence of inflammatory reaction around the ulcers, which show necrotic sloughing and tend to develop secondary infection. The condition progresses extremely rapidly to a fatal termination in two to five days, so that it is an urgent necessity to make an early diagnosis in order that appropriate treatment can be instituted at once. Since *sulphonamide* derivatives are usually given to counteract infection, often with pyrexia, as in puerperal fever, colds, influenza, sore throats, the change to agranulocytosis is often not observed until too late: hence the absolute importance of regular blood counts during the use of all these toxic drugs. The onset of the neutropenic state is noted by the fall in the total white cell count to 1000 or less, affecting the granular white cells (polymorphonuclear cells) which may be reduced to nil or only a few per cent. There is little or no anæmia

or thrombocytopenia, which helps to differentiate the condition from aplastic anæmia and thrombocytopenic purpura.

HÆMORRHAGIC DISORDERS

The hæmorrhagic disorders of the blood (Wilkinson, 1940) include (a) the *hereditary hæmorrhagic conditions* of hæmophilia, hereditary hæmorrhagic diathesis, hereditary capillary telangiectasis and constitutional fibrinopenia. The diagnosis of these is easy, since they exist from birth and are characterized by recurrent hæmorrhages into the joints and from the mucous membranes, and are often seen in several members of one family. Examination of the bleeding time, coagulation time, platelet count, and blood fibrinogen serve to confirm the appropriate diagnosis.

(b) *The purpuras* include thrombocytopenic purpura, both primary and secondary, and the so-called anaphylactoid or Henoch-Schönlein purpura. These are very important and are relatively frequent in occurrence.

Thrombocytopenic purpura usually comes on quite suddenly, sometimes acutely, after exposure to toxic agents, such as benzene, gold, arsenic, bismuth, the sulphonamide derivatives, barbiturates, amidopyrine, or radium, although the idiopathic type has often a more chronic and insidious onset. The first symptoms are recurrent unexplained bruisings and recurrent petechial hæmorrhages of varying severity in the skin and mucous membranes, sometimes going on to large ecchymoses, retinal or cerebral hæmorrhages, and hæmorrhages from the gastro-intestinal (hæmatemesis, melæna) or genito-urinary (e.g. hæmaturia) tracts. The persistence or recurrence of these hæmorrhagic manifestations may lead to gross secondary anæmia which is associated with severe thrombocytopenia (often below 40,000 per c.mm.), prolonged bleeding time, normal coagulation time, poor clot retraction, normal gastric secretion; splenomegaly is often found, whilst sternal marrow biopsy shows very few platelets or megakaryocytes. After splenectomy, which cures the primary type, but not that secondary to toxic agents, the whole condition clears up and the blood returns to normal.

The anaphylactoid or Henoch-Schönlein type of purpura is characterized by varying degrees of urticaria, swollen joints, intestinal colic, diarrhœa, constipation, severe ecchymoses of the skin, or purpuric manifestations in the mucous membranes of the alimentary or genito-urinary tracts, and severe rheumatic pains in the limbs. The condition is very chronic and as a rule begins in the second or third decade, recurring at frequent intervals throughout life. It is most resistant to treatment. All hæmatological investigations are as a rule negative.

(c) *Hæmorrhagic deficiency diseases* include scurvy and melæna neonatorum. The former is well known and starts with petechial hæmorrhages, sometimes more extensive ecchymoses and spongy gums, and is due to a deficiency of ascorbic acid in the diet; there may be a severe anæmia often of the megalocytic type.

In melæna neonatorum (hypoprothrombinæmia) or hæmorrhagic disease

colour should serve as a warning; a sternal marrow biopsy will invariably indicate the leukæmic nature of the condition, which in the course of a few days or weeks runs to a fatal termination, before which, however, the peripheral blood will show more typical features of an acute leukæmia.

A relatively rare condition, *acute monocytic leukæmia*, is seen from time to time—its onset is quite characteristic. In most cases it starts insidiously with some lack of energy and general fatigue; then a peculiar maroon coloured œdematous swelling of the gums resembling scurvy is noted with fetor of the breath: this frequently appears to follow tooth extraction and may be associated by the patient with the oral condition, the true nature of the disease not being at first recognized. The condition progresses rapidly, the gums continuing to swell so that the teeth are completely covered with the mass of bluish or maroon coloured swollen gum which does not respond to any local or general treatment. The spleen and lymph glands are not enlarged but examination of the blood shows a slowly rising total white cell count and a rapidly increasing number of monocytes and monoblasts, so that the differential white cell count shows ultimately 90 per cent. or more of these latter with a total count of 40,000 to 100,000 per c.mm. There is a variable degree of anæmia. The condition is rapidly fatal in a few weeks. No other condition shows this characteristic onset, progress and blood picture. The sternal marrow shows a picture closely resembling the peripheral blood smear.

AGRANULOCYTOSIS

Owing to its etiology, agranulocytosis, or malignant neutropenia, may present some difficulties in the early stages of its onset. As a rule it is a result of exposure to some toxic agent, such as the sulphonamide derivatives, barbiturates, amidopyrine, preparations of gold, arsenic, bismuth, benzene, thiouracil, and many other similar therapeutic drugs.

The first symptoms are usually pyrexia, then soreness and necrotic ulceration of the mucous membranes of the throat, mouth and fauces, followed by brawny swelling of the neck. Sometimes the necrotic ulceration appears first or solely in the mucous membranes of the rectum or vagina. There is no evidence of inflammatory reaction around the ulcers, which show necrotic sloughing and tend to develop secondary infection. The condition progresses extremely rapidly to a fatal termination in two to five days, so that it is an urgent necessity to make an early diagnosis in order that appropriate treatment can be instituted at once. Since sulphonamide derivatives are usually given to counteract infection, often with pyrexia, as in puerperal fever, colds, influenza, sore throats, the change to agranulocytosis is often not observed until too late: hence the absolute importance of regular blood counts during the use of all these toxic drugs. The onset of the neutropenic state is noted by the fall in the total white cell count to 1000 or less, affecting the granular white cells (polymorphonuclear cells) which may be reduced to nil or only a few per cent. There is little or no anæmia

There is no complaint of pain, but in certain anæmias associated with achylia, such as pernicious anæmia and hypochromic microcytic anæmia, flatulent dyspepsia with a feeling of distension after meals and some nausea, loss of appetite, diarrhœa or constipation are commonly noted, whilst early complaint may be made of recurrent soreness and ulceration of the tongue and mouth, often put down to bad teeth or smoking or condiments. The acute onset of necrotic ulceration of the mucous membranes of the pharynx, buccal cavity, fauces, rectum or vagina (often with brawny swelling of the neck and moist sounds at both bases of the lungs) indicates an acute agranulocytosis. In acute leukæmias, ulceration of the gums may occur with petechial hæmorrhages, whilst the characteristic purplish œdematous swelling of the gums, resembling scurvy in many respects, is noted in acute monocytic leukæmia.

Dysphagia associated with achlorhydria, as in the Plummer-Vinson syndrome, and koilonychia are pathognomonic features of microcytic hypo-chromic anæmia and of no other blood disease. Loss of weight may frequently occur in many of the anæmias but is not usual in the microcytic hypochromic anæmias, in which weight may be increased, often in association with some degree of hypothyroidism.

Neurological symptoms and signs are seen only in association with pernicious anæmia and not other megalocytic anæmias: a distinguishing feature from achrestic anæmia, in which there is also a normal gastric acidity.

A Raynaud type of phenomenon with erythromelalgia may occasionally be the first signs in polycythæmia, although the most common symptom is recurrent headaches with splenomegaly.

Common to most severe anæmias, and therefore not specific, are the changes in the cardiovascular and respiratory systems, namely, cardiac dilatation, hæmic systolic bruits, some tachycardia and palpitation, low blood pressure (rising with treatment), sometimes œdema of the ankles and dyspnœa.

Splenomegaly may be noted in many of the conditions discussed, but to a varying degree. Gross enlargement is seen in Banti's syndrome, Gaucher's disease and allied lipoid dysfunctions, chronic myeloid and lymphatic leukæmias. Less marked enlargement is seen in polycythæmia, hæmolytic anæmias, thrombocytopenic purpura. Little or no enlargement may be seen in pernicious anæmia, microcytic hypochromic anæmia and acute leukæmias. The occurrence of splenomegaly in Hodgkin's disease, glandular fever, subacute bacterial endocarditis, malaria and certain other typical and infective conditions must be borne in mind when considering the diagnosis of these anæmias.

References

Wilkinson, J. F. (1936): *Brit. Encyc. med. Pract.*, **1**, 408.
—— (1940): *The Practitioner*, **145**, 382.
—— (1945): *Ibid.*, **155**, 329.

of the newborn—as distinct from the "hæmolytic" disease of the newborn or erythroblastosis—there is a deficiency of vitamin K and hence of prothrombin in the blood so that the blood does not coagulate normally, thus leading to spontaneous hæmorrhages from the stomach, bowel, umbilicus, renal tract, and skin in infants of a few days old. Diagnosis depends upon this history and the finding of hypoprothrombinæmia.

DISORDERS OF THE BLOOD ASSOCIATED WITH GROSS SPLENOMEGALY

A number of diseases of the blood are characterized clinically by marked and sometimes gross enlargement of the spleen.

Of these the most important one is the so-called *Banti's syndrome* ("splenic anæmia") which is usually first noted on account of complaints of marked lack of energy, weakness and general debility for a long time. Blood examination shows a non-specific mild anæmia of perhaps $3-4 \times 10^6$ red cells per c.mm., hæmoglobin 70–80 per cent., and slight leucopenia or a normal count, the remaining hæmatological findings being normal. There is a varying degree of usually painless splenic enlargement, which may be very gross in some patients, with or without some hepatic enlargement.

Sometimes the first symptom in this condition is a hæmatemesis which may recur at intervals, and ultimately it can often be demonstrated by a barium swallow radiograph that this comes from varices, usually at the lower end of the œsophagus. In my experience this condition has become much more common in the last few years.

Gross splenomegaly, often with hepatic enlargement, is commonly seen in the lipoidoses; of these *Gaucher's disease* (lipoid-kerasin) is characterized by the occurrence of brownish skin pigmentation, pingueculæ, typical bone changes, variable anæmia with the usual symptoms associated with such, whilst sternal marrow shows the Gaucher's cells in the smears.

Niemann-Pick's disease is associated with disturbances of metabolism of the lipoid-sphingomyelin; there are no bony changes but gross enlargement of spleen and liver are noted with the usual symptoms of anæmia.

Both these conditions are seen most commonly in Jewish children.

Xanthomatosis or *Hans-Schuller-Christian disease* shows similar features, deposition of cholesterol and its derivatives, and typical bone changes. The diagnosis of all these three lipoidoses is confirmed by chemical examination of the blood and spleen, and by sternal marrow biopsy.

CONCLUSION

Reviewing the points considered above, it will be seen that the most common early symptoms and signs associated with disorders of the blood are those of an insidious and gradually increasing tiredness, lack of energy, shortness of breath and palpitation on exertion, with perhaps some loss of weight.

drug may be given intramuscularly in the usual dosage (0.5 to 2 c.cm.) should digitalis alone fail to relieve congestion.

Diet.—During the first few days the diet need consist of no more than fluids (glucose and orange juice, milk, weak sweet tea) in moderate quantity. As acute symptoms subside the patient may be allowed a light, dry, low-residue diet of easily assimilated type, such as is in general use for cases of congestive heart failure. Meals should be small and frequent rather than bulky, and should contain a sufficiency of protein without roughage.

Bowels.—The morphine given at the outset may inhibit bowel action for a day or two; this is not important. When acute symptoms have subsided the bowels should be gently opened, using mild aperients rather than drastic purgatives. Four ounces of olive oil instilled into the rectum at night followed by a small rectal wash-out next morning is a safe procedure when constipation has been present for some days.

After-care.—Six weeks' rest in bed should be insisted on, even in mild cases, despite the protestations of a patient who may look and feel well after the first few days. There are definite risks throughout this period (recurrence; ventricular fibrillation; onset of failure; peripheral embolism; rupture of the infarct) and although these disastrous complications cannot be entirely prevented, their incidence is lessened by strict observation of the six weeks' rule. By the end of the fifth week *from the cessation of pain* the patient should be able to sit up a little in bed, e.g., for meals, and during the sixth week, if free from pain, he may be allowed to wash and shave himself and to move more freely about in bed. Once the patient is up and about, convalescence for a month should be advised. The date of return to work will depend *inter alia* upon his condition and upon the nature of his employment. He should be supervised on the same lines as a patient with angina pectoris.

ANGINA PECTORIS

The treatment of angina pectoris is much more a matter of general management than of drug therapy. The most useful measure in the average case is *weight reduction.* The patient is commonly of thick-set or stout build, exceeding the ideal weight for age, sex and height by a couple of stones. The loss of this excess should be attempted by simple dietetic restriction. Thyroid should not be used in view of its liability to aggravate the angina.

Individual consideration of the *mode of life and environment* of the patient is of utmost importance. In professional men, ruthless pruning of business and social commitments to the bare essentials may greatly lessen or even abolish symptoms. For skilled workers similarly, employment may be found whereby the experience of the craftsman is utilized while younger assistants carry out the actual labour involved. Unskilled workers may be less fortunate, in that incapacity of similar degree may prove for them a total disability. Employment involving possible risk to others should not be permitted to sufferers from angina.

As at work, so in the home: by taking thought avoidable effort can be reduced to the minimum and the patient taught to live within his effort capacity. Eight hours in bed each night and restful weekends are within the reach of all patients.

Rest in bed.—Cases of angina of recent onset are frequently much improved by an initial period of two to three weeks rest in bed. Such patients may be allowed more liberty than the subjects of a coronary occlusion and may rise for toilet purposes.

Vasodilators.—As an adjunct to general treatment nitrites are of value. Nitroglycerin (tablets of glyceryl trinitrate, *B.P.*) is preferable to amyl nitrite for routine use. Dosage is more accurately controlled; the tablets are easily carried, and can be used without rendering the sufferer conspicuous in public; and some cases resistant to amyl nitrite respond well to nitroglycerin. The tablets should be fresh, and

REVISION CORNER

This section is devoted to short articles in which experts summarize modern treatment and clinical procedures, particularly for the benefit of general practitioners who have returned from the Forces.

THE TREATMENT OF CORONARY THROMBOSIS AND ANGINA PECTORIS

CORONARY THROMBOSIS

Rest and sedation:—Rest in bed is imperative, together with measures to relieve pain. It is wiser to nurse such patients in a hospital or nursing-home from the outset, unless the home circumstances permit of the services of two strong nurses. Rest in bed must be complete: the patient should be fed and washed, and should use a urinal and if possible a bedpan. In certain cases it is wiser to allow the use of a night commode placed beside the bed, as likely to provoke less exertion than efforts to use a bedpan.

Pain calls for morphine, which may be given safely at any stage of the attack. One-quarter of a grain (16 mgm.) hypodermically is seldom enough to relieve the pain, and a larger initial dose, $\frac{1}{3}$ or even $\frac{1}{2}$ grain, (22 mgm. or 32 mgm.) may be given. The drug may be repeated at intervals of two to four hours, depending upon the dose given, until pain is relieved. The usual precautions apply regarding total dosage and the dangers of repeated injections in shocked patients.

Anticoagulants.—Attempts have been made to prevent extension of the thrombosis by the use of anticoagulants (heparin; dicoumarin). The risks involved are not balanced by demonstrable benefits, and their use is not advocated.

Vasodilators.—Dilators of the nitrite group (nitroglycerin, amyl nitrite) do not relieve pain in cases of occlusion and tend to exaggerate temporarily the fall in blood pressure already present in severe cases. Their use is contraindicated.

Oxygen.—In patients profoundly shocked, or in great distress from dyspnœa or pain, oxygen in high concentrations is often of striking value. It should be given continuously by B.L.B. mask, using a rate of flow of 6 to 8 litres per minute with all ports closed. The alveolar O_2 concentration may thus be raised to 80 or 90 per cent., and kept at that level for many hours or a day or two.

Digitalis.—The onset of congestive failure is the indication for the administration of digitalis. Caution is necessary during the first week after an infarction, for the drug may increase extrasystolic irregularities and predispose to ventricular paroxysmal tachycardia during this critical period. Failure developing in the second week or later may be safely treated along standard lines. The onset of auricular fibrillation with a high ventricular rate may also call for digitalis in full doses.

Quinidine sulphate, in doses of 3 to 5 grains (0.2 gm. to 0.32 gm.) four-hourly, is useful in controlling ventricular paroxysmal tachycardia when this has developed, or for patients in whom gross extrasystolic disturbances of rhythm indicate its imminence. In some clinics quinidine in small doses is given as a routine to all patients during the first week, as a prophylactic against these dangerous ectopic rhythms.

Aminophylline (theophylline with ethylenediamine) is useful for the relief of dyspnœic failure, cardiac asthma and Cheyne-Stokes breathing, should such occur. The action is most striking when given intravenously (0.25 to 0.5 gm.), but the drug must be given *slowly* and well diluted with saline (10 to 20 c.cm.). The injection should be temporarily interrupted during the hyperpnœic phase of periodic breathing. The action is transient and injections may be repeated several times a day. Oral administration (0.1 gm. in tablet) is less effective.

Mersalyl.—Diuretics are unnecessary except when failure with peripheral or pulmonary congestion has developed. The outlook in such cases is generally bad. The

the bladder, for, as a result of this, a patient whose urine is sterile almost inevitably becomes infected. Indeed, this common occurrence is one of the reasons why this double operation should carry a lower mortality than the one-stage operation, for the patient is thereby given time to build up an immunity to infection before he has to submit to prostatectomy. But in another group of cases cystotomy carries heavier risks, for a patient with a high degree of retention and renal impairment has to survive the effects of decompression and, however carefully this is done, there is the same probability of infection. In bad cases the two together may well prove fatal. When, however, the patient has come through this stage, and when his renal function is improved and shows, if not a normal, at least a stable blood urea, then the chances that prostatectomy can be carried out safely are good. It can therefore be said that to-day prostatectomy in two stages, despite its obvious dangers and disadvantages, remains a sound procedure and one that should not be lightly abandoned, particularly by those surgeons who have to treat such patients in surroundings not suited to specialized surgery. Bilateral vasotomy should be performed at the time of the cystotomy.

The next method which may be mentioned is that of *perurethral prostatic resection.* This can be done either by the punch method or with the diathermy resectoscope. Both methods are good. The punch operation has the disadvantage that the instrument is a large one and therefore sometimes requires to be introduced through an incision in the bulb of the urethra. The use of the diathermy carries more risk of infection, but fortunately this is usually strictly localized to the area of the operation; it affects the bladder but little and rarely makes the patient ill. Resection is undoubtedly the operation of choice in cases of fibrous bar at the internal urinary meatus, and also when the prostate is small though obstructive. After operation, a tied-in catheter is necessary for only a few days and sometimes only for twenty-four hours; the patient has no pain, and quickly returns to his work. It is a difficult operation and one which requires much experience on the part of the surgeon if it is to be ensured that enough of the obstructing gland, and yet not too much, is removed. The diathermy instruments are, moreover, delicate and expensive. For these reasons this method should be avoided by a surgeon who is not prepared to make a special study of the technique. Either method can be used to resect large prostates, but the operation is then decidedly more difficult and makes considerable demands upon the surgeon's endurance. In such cases it is often wise to be content to treat half the prostate at the first operation and then complete the resection a few days later. A considerable amount of blood may be lost, and transfusion may be required. Patients with chronic obstruction have first to be dealt with by appropriate methods of catheterization or cystotomy, before resection is undertaken.

Millin's retropubic prostatectomy is now becoming widely practised. In this operation the bladder is not opened. The anterior surface of the prostatic capsule is exposed with the patient in a slightly head-down position. The vessels lying upon it are tied or coagulated by diathermy; the capsule and coverings down to the adenoma are incised and then enucleation is performed. After this, the vesical neck is carefully examined and a wedge may be cut out of it. Hæmorrhage from the prostatic bed is arrested by diathermy, and the incision through the capsule is sutured after a catheter has been introduced into the bladder through the urethra. The prevesical space is drained through the abdominal incision.

The operation is a good one and, although those who practise it are sure, as in any other operation, to meet with difficulties from time to time, and particularly in their earlier cases, the results promise to be excellent. The obvious danger to life lies in sepsis in the prostatic region, which may give rise to emboli from the veins or to pelvic cellulitis, for this operation is akin to that of Harris in that sutures are inserted which pass through the lumen of a part of the urinary tract and also through the cave of Retzius. If organisms are present in the urine at the time of operation or

should be sucked or chewed rather than swallowed, since absorption from the buccal mucosa is rapid. The usual effective dose is 1/100 grain (0.65 mgm.), but in some cases a smaller dose [1/200 grain (0.32 mgm.) or less] is effective, whereas others may require 1/50 or even 1/25 grain (0.13 mgm. or 0.26 mgm.) for relief. The tablets should not only be taken whenever pain is felt, but the patient is instructed to suck a tablet a few minutes before performing some essential act which habitually provokes pain, e.g., before going to stool, or going upstairs to bed, or attending a committee meeting. In severe cases up to 20 to 25 tablets may be taken daily.

Other vasodilators have been used. Alcohol has a beneficial action in many cases, but its use is attended by the undesirable risk of habit; so, too, morphine, which is very effective, should not be used in angina, since addiction is a grave risk. Drugs of the caffeine group have a vasodilator action and theobromine, 5 grains (0.32 gm.), is frequently prescribed, usually with phenobarbitone, ½ grain (32 mgm.). Nicotinic acid has also been used in recent years but without dramatic success. There is no evidence that these drugs can rival, far less replace, nitroglycerin. Muscle and tissue extracts are likewise of little value.

Surgery.—In patients experiencing intractable pain on the slightest exertion, not adequately controlled by full dosage of vasodilators and necessitating repeated use of morphine, the question of surgical aid must be considered. Resection of the stellate ganglion or paravertebral injections of novocain or alcohol, may render a life of tolerable comfort possible in cases of distressing *angina decubitus*. The value of surgical measures in general, however, is limited, and in this country conservative treatment is the rule for all but a small minority of cases.

<div align="right">Ian G. W. Hill, C.B.E., M.B., F.R.C.P.Ed.</div>

THE TREATMENT OF BENIGN ENLARGEMENT OF THE PROSTATE

Treatment has passed through several phases since Freyer caused operative methods to be widely used for this condition. It is, however, worth remembering that his mortality rate in a series of 1,337 cases of prostatectomy was given as 4.77 per cent. This was before 1920, and therefore at a time when sulphonamides, penicillin and blood transfusion were not yet available and when anæsthesia was relatively crude.

SURGICAL PROCEDURES

Operation in one form or other remains the method of choice in treatment, for although endocrines have done much for carcinoma of the prostate they are so far without certain value in simple enlargement of the gland. It is unfortunate that this is not appreciated by all doctors, for the indiscriminate administration of stilbœstrol to patients in whom the diagnosis is uncertain sometimes results in making it more obscure.

Simple enucleation of the enlarged gland, commonly known as *Freyer's prostatectomy in one stage*, is still widely practised. The mortality rate for this operation is often unsatisfactory, particularly when performed by some surgeons, and upon patients who are subsequently cared for by residents and nurses with little experience and even less interest in such procedures. And it may here be pointed out that without good nursing any method of prostatectomy is bound to spell disaster for a proportion of the cases. The more complicated operations used to-day demand nursing, not perhaps so exacting, but none the less of the highest quality if success is to be won.

Freyer's prostatectomy in two stages, that is to say, cystotomy followed after an appropriate interval by enucleation, is relatively a much safer procedure. Often in serious cases the most dangerous stage is the operation which provides drainage of

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Acid Phosphatase in Prostatic Carcinoma

QUERY.—I should be grateful if you could explain to me briefly the nature of, actions of, and difference between acid and alkaline phosphatase. Is there any known reason, or even theory, why the acid phosphatase level in the blood plasma should be affected in prostatic cancer with bone metastasis? Why should the concentration of acid phosphatase be so very high in seminal fluid?

REPLY.—The acid phosphatase in the plasma can be regarded as an index of prostatic activity, and carcinoma of the prostate is the type of tumour which secretes what might be termed the "active principle of the gland", and therefore it spills over, so to speak, into the plasma. Whether it is increased more in the case of bone metastasis because the growth is more active, or whether it is due to a direct action in the bone itself, cannot at present be answered. Likewise, on the basis of present knowledge, it is not possible to say why the acid phosphatase is so high in the seminal fluid. We are only just beginning to understand how complicated is the process of fertilization in the mammal, and the human subject in particular. The action of hyaluronidase indicates that there are all kinds of complicated reactions going on prior to fertilization, and it might well be that the phosphatase of the seminal fluid plays an important part.

PROFESSOR E. C. DODDS, M.V.O., M.D., F.R.C.P., F.R.S.

A Clinical Conundrum

QUERY.—The patient, a woman of about forty years of age, some twelve to fourteen years ago had an operation for removal of the fallopian tubes and almost complete removal of both ovaries, only a very small part of one ovary being left. She made a very good recovery from this operation and has been menstruating regularly ever since. She continued in good health up to about five or six years ago when she complained of urinary trouble. X-rays showed shadows in both kidneys. Inflammatory and localizing symptoms in the right kidney necessitated its removal. The excised kidney was found to be much enlarged and contained several stones with great damage to kidney tissue. Recovery was uneventful. She again continued well up to three years ago when she had a further set back. This time it was a

fracture of one of the metacarpal bones sustained for very little cause. X-rays showed several oval shadows in many bones of the hand, labelled enchondromas by the radiologist. Recovery from the fracture was complete.

I now come to the last phase. About three weeks ago the patient complained of lumbosacral pain. On examination, a kyphosis of the lower dorsal spine was found with tenderness of the affected vertebræ. Another X-ray revealed a condition of the spinal and pelvic bones similar to those of the hands. The label this time is "multiple enchondromas of skeleton". I presume the pain is due to pressure on the posterior nerve roots, this also being the cause of patches of paræsthesia which are present in the lower extremities. I am wondering if the renal calculi and the enchondromas are connected with each other? I shall be grateful if you will advise me as to what line of treatment is advisable in this case. The patient's general health is good.

REPLY.—The gynæcological history has probably no bearing on the subsequent events which were, in brief, bilateral renal calculi five years ago, pathological fracture of a metacarpal three years ago, and collapse of a dorsal vertebra a month ago.

The X-ray diagnosis of multiple enchondromas presumably means that a number of clear areas were seen in the bones of the hand, and later in the vertebral bodies and pelvis, in fact, in all the bones that were examined. Such areas mean no more than that the radio-opaque bone is being replaced by some non-radio-opaque tissue. That chondromas should appear in all parts of the skeleton in a woman aged forty is extremely unlikely. Multiple chondromas are seldom seen except as congenital malformations in the hands and feet of children, and the chondromas appearing in adult life are usually single and massive and are chondro-sarcomas rather than simple tumours.

Multiple clear areas appearing in the bones of an adult and leading to pathological fracture, suggest three things: secondary deposits from some undiscovered carcinoma, myelomatosis, or multiple cysts in bone due to an adenoma of the parathyroid. Bone metastases may occur in carcinomas of almost any organ, those most commonly encountered being growths of the breast, stomach, thyroid and adrenals. Multiple secondary deposits causing pathological fracture in a patient who appears perfectly well and has no localizing symptoms may be seen when the

gain access subsequently, then a serious danger is present. Millin drains this region more consistently than was considered necessary by Harris. To-day, however, this risk is greatly lessened, for when Harris devised his operation of prostatectomy with retrigonization and obliteration of the prostatic fossa, sulphonamides were not available. He had urged the most extreme caution to prevent the occurrence of sepsis, and stressed the inevitable risks if it should occur, but despite his warnings most of the fatal results arising in his operation were due to this. Although sulphonamide treatment in various improved forms is now to hand, it remains true that sepsis within the pelvis is an ever-present danger in the operations of Harris and Millin, yet it is one which can be minimized with modern drugs and if the technique of the originators of these operations is carefully followed.

Prostatectomy by an open transvesical approach was first developed in this country by Thomson-Walker. In this operation, after the bladder cavity had been inspected and the prostate enucleated, an attempt was made to control bleeding by suture of the vesico-prostatic margin. The operation had two disadvantages: the arrest of hæmorrhage was often very imperfect; also, if the bladder was uninfected at the time of operation it commonly became so afterwards, and, for the same reason, if it was already infected new strains of bacteria might be added. None the less, it was blood loss during and after operation which was the chief defect in this method, for the danger from infection, when it occurred, was mitigated by good bladder drainage. Deep pelvic sepsis was rarely seen, for the extravesical tissues were but little opened up.

Wilson Hey's operation, which he names *aseptic prostatectomy*, is a serious, and it seems successful, attempt to prevent infection from reaching the area of operation. The bladder is opened suprapubically and after the prostate has been enucleated a large part of the trigone is resected to give good access to the prostatic fossa. Hæmostasis is now achieved by forcep pressure and diathermy coagulation, no ligatures being used. Next, a urethral tube, guided by a small catheter, is passed in a retrograde manner and placed in position to provide bladder drainage, and then the bladder is closed by three layers of sutures. A drain is put through the abdominal wall for twenty-four hours and, except for the removal of this, the wound is not uncovered until the stitches are taken out on the tenth day. The urethral tube is usually withdrawn on the fourth day, and micturition is then resumed. Complete closure of the bladder is made safe because bleeding has been largely arrested, but the great advantage of this is that there now remains only the urethral path for invasion of a sterile bladder by bacteria, or for the introduction of a fresh infection when cystitis already exists. Hey endeavours to prevent this by not operating until an interval of at least three weeks has elapsed after the passage of a catheter or cystoscope by the retrograde manner in which he puts the urethral tube into position, and by its early removal. Sulphonamide derivatives are also used, together with other special methods when required. His results justify his endeavours, and the asepsis achieved enables the method to be used even in cases of severe chronic obstruction and with incipient uræmia. However, it is not easy to see that the method is applicable to those patients whose bladders, having lost all tone as a result of over-distension, are commonly considered to require a prolonged period of continuous drainage for recovery of function.

CONCLUSION

A fair appreciation of the position of prostatic surgery to-day is to state that the two new operations deserve to be increasingly practised, that perurethral resection is of proved value and gives good results with low risks, and that Freyer's prostatectomy in two stages still retains a worthy place. Sulphonamides and penicillin, used both for prophylaxis and in the treatment of infection, associated with improved anæsthesia and blood transfusion when required, have made great advances possible.

R. Ogier Ward, D.S.O., O.B.E., M.C., M.Ch., F.R.C.S.

baby will not suit another. The best infant's nurse is not one who has been trained to obey some rigid system or set of rules, but one who has learnt to be all things to all babies. As to misery in the infant comparable to the unhappi-

ness of the absent lover or the exile from home, I am not so sure. The cry of the baby is a response to stimuli of cold, heat, hunger or peristaltic contraction. The baby is unconscious of all else.

PRACTICAL NOTES

Diabetes Mellitus in Norway

AN analysis by P. Hanssen (*Acta Medica Scandinavica*, 1946, Supplement 178) of the cases of diabetes mellitus occurring in Bergen, a town of 100,000 inhabitants, during the period 1925-1941, provides some interesting data. The number of diabetic patients during this period was 794, of whom 402 were still alive in 1941. In this year the number of diabetics was 3.8 per 1,000 of the population (3.2 per 1,000 for males and 4.3 per 1,000 for females). During the period covered by the study there was a steady rise in the incidence rate: in 1925 there were between 100 and 180 diabetics; in 1934 the figure had risen to between 300 and 350, whilst in 1940 it was 400. A comparison of the mortality among diabetic subjects with the general mortality in Norway gave the following figures: in the period 1925-1934 the mortality among male diabetics was 4·7 x the expected mortality rate, and among female diabetics it was 3·2 x the expected mortality. In the period 1934-1942 the corresponding figures were 2·7 and 2·3. This "excess mortality" for diabetics was greatest in the younger age-groups and decreased with age. Sixty cases of diabetic coma occurred during the period under investigation, and the mortality rate among these was 40 per cent.; these deaths represented 8·2 per cent. of all diabetic deaths. Hypertension was rare under the age of fifty; above this age a systolic pressure of over 160 mm. Hg was found in 43 per cent. of males and 68 per cent. of females, whilst a diastolic pressure of over 100 mm. Hg was found in 25 per cent. of males and in 36 per cent. of females. Among 104 diabetics examined during 1940-1941, there were 18 with diabetic retinitis. Pulmonary tuberculosis was responsible for 4·1 per cent. of the deaths among diabetics.

Ringworm of the Scalp

A SERIES of articles on the treatment of ringworm of the scalp (*Journal of the American Medical Association*, September 14, 1946, **132**, 58, 62, 65, 67) gives an evaluation, based upon the cure rate, of different methods of local therapy. L. Schwartz *et al.* obtained a cure rate of 84 per cent. by the use of salicylanilide ointment (salicylanilide 5 per cent. in carbowax 1,500). The selection of this medicament followed a comparative trial with a number of other local

applications. A note attached by the Medical Officer of Washington County states that salicylanilide ointment is at present being used exclusively in the treatment of tinea capitis with highly satisfactory results, and that by this means the infection can be controlled without excluding the child from school during the period of treatment. G. M. Lewis *et al.*, following an estimation of the value of local endocrine therapy, record disappointing results with testosterone, œstradiol and diethylstilbœstrol, and advocate the use of X-ray therapy, a measure which resulted in their series in a cure rate of 90 per cent. The fungicides, including streptothricin (J. Lowry Miller *et al.*) proved disappointing, but a cure rate of 64 per cent. was obtained by A. Strickler, who used iodine enhanced by the application of photosynthesis. The mixture employed was: iodine 78 per cent., red blood cells 2 per cent., sodium chloride 1.9 per cent., chlorophyll (2 per cent. in isotonic solution of sodium chloride) 0.07 per cent., deceresol 10 per cent., magnesium dioxide 8 per cent., and spleen extract 0·005 per cent., incorporated in an oily vehicle, in the amount of 2 gm. of the mixture to 30 gm. oil (cottonseed oil). After clipping the hair, acetic acid is rubbed into the scalp by means of a toothbrush for two minutes; an electric bulb (150 to 200 watt) is then kept sufficiently close to the scalp to generate heat for two minutes, then the iodine and oil combination is rubbed in with friction, using another toothbrush, and heat is again applied locally for six minutes.

Contramine in the Treatment of Herpes Zoster

SATISFACTORY results from the use of contramine (diethyl - ammonium - diethyl - dithio - carbamate) in the treatment of sixteen patients with herpes zoster are reported by D. N. Bengis (*South African Medical Journal*, August 24, 1946, **20**, 467). The preparation was given intramuscularly in doses of 0.125 gm. per c.cm., one injection being given daily until pain had subsided, with a maximum of six injections. In most cases there was rapid relief of pain, the duration varying from one day (in one case) to seven days (in one case). The average number of injections required was three. In addition to alleviation of pain there was fairly rapid drying

primary growth is a neuroblastoma or a silent bronchial carcinoma. Myelomatosis is usually characterized by severe pain of rheumatic type. The diagnosis would be confirmed by the discovery of Bence-Jones albumose in the urine.

The conjunction of renal calculi with clear areas in bone strongly suggests that the cause of the syndrome is a parathyroid tumour. The investigations required are an estimation of the calcium metabolism, and a careful examination of the neck for a rounded tumour in the region of the thyroid. If the figures for serum calcium and phosphatase are raised and that for serum phosphorus low, and if the urinary output of calcium is high, a parathyroid tumour can be assumed to be present even though no lump can be felt, and the neck should be explored.

Other investigations that might assist the diagnosis if the figures for calcium metabolism are within the normal range, are an X-ray of the chest, and the removal of the tissue from an accessible area in one of the surface bones for section.

HENEAGE OGILVIE, K.B.E., D.M., CH.M., F.R.C.S.

The Physiology of Hiccough and Yawning

QUERY.—Is anything known of the physiology of (a) hiccough, and (b) yawning?

REPLY.—*Hiccough.*—This is an involuntary spasmodic contraction of the diaphragm. It is usually reflex in action due to impulses passing down the phrenic nerve from the respiratory centre, the afferent path probably travelling with the vagus. The stimulus preceding the reflex response is gastric irritation, possibly from distension, possibly fermentation. In addition to the normal type of hiccough, epidemic hiccough occurs, and other unusual types, together with cases of long-standing hiccoughing in individuals. In all these, a toxic irritation of the phrenic nerve cells or endings appears to be the mechanism. One of the best methods of treatment is to inspire 6-7 per cent. CO_2.

Yawning.—Yawning is a spasmodic prolonged inspiratory act associated with fatigue of the respiratory centres. The respiratory centre (pneumo-toxic centre of Lumsden) appears to become relatively quiescent in certain lethargic atmospheres associated with mental fatigue. The respiratory centre in consequence develops a high threshold to normal stimuli. The stimuli increasing, overcome the threshold and produce a spasmodic prolonged inspiration (apneusis). If ennui be dissipated by the subject's attention being excited, the respiratory centres become more responsive and return to their normal excitability, and yawning ceases. In extreme cases,

the inspiratory spasm of yawning is associated with spasm of other muscles throughout the body leading to stretching, not only of the jaw muscles, but also of the limbs; this is an example of irradiation within the central nervous system to other motor centres.

Loneliness of the Newly Born

THE Vicar of Latton, Wilts. writes:—The loneliness of the newly born child who has been within his mother's body for months and who from birth is denied contact with that body must far surpass that of home-sickness or love-sickness. Yet in maternity hospitals the child is removed from the mother and only restored to her at feeding time. No mother save the human mother would tolerate such a state of affairs. I am therefore rejoiced to read that owing to lack of staff and accommodation in maternity hospitals there is every likelihood of home nursing becoming almost universal.

Dr. Hector Cameron, to whom this letter was shown, comments as follows:—There is an element of truth in the vicar's contention. It is, no doubt, the function of all mammalian mother animals to lie on their young, so that by contact with their warm bodies they may preserve the unstable temperature of the newly born within normal limits. If the cat forsakes her kittens, none will survive. If the baby is to lie in a separate cot apart from its mother, some form of artificial warmth may be necessary. Very often, it is true, we find that the human infant, restless and emotional in its cot, will at once become quiet and drowsy when taken into the mother's bed, up against the comfortable warmth of her body. The young of no other animal displays the degree of emotional unrest which the human infant with its complex nervous organization so often displays, and the cry of her baby is a sound which nearly always profoundly disturbs the mother's peace of mind. The mother has just come through an experience which causes much greater exhaustion to her than to creatures less highly evolved. Her need for rest is very great. At the best her sleep must be interrupted at intervals by the necessity of suckling the child. It is usually wise that she should not be subjected to the disturbance caused by a restless infant. The matter is complicated by the fact that nowadays in hospitals and nursing homes several women commonly share a room and if all their infants were constantly with them the interruption would be well nigh continuous. Babies to-day in hospitals or in home are born in artificial circumstances; we cannot reproduce the conditions of the wild. In the management of a matter of this kind there can be no rigid routine. What suits one

baby will not suit another. The best infant's nurse is not one who has been trained to obey some rigid system or set of rules, but one who has learnt to be all things to all babies. As to misery in the infant comparable to the unhappiness of the absent lover or the exile from home, I am not so sure. The cry of the baby is a response to stimuli of cold, heat, hunger or peristaltic contraction. The baby is unconscious of all else.

PRACTICAL NOTES

Diabetes Mellitus in Norway

AN analysis by P. Hanssen (*Acta Medica Scandinavica*, 1946, Supplement 178) of the cases of diabetes mellitus occurring in Bergen, a town of 100,000 inhabitants, during the period 1925-1941, provides some interesting data. The number of diabetic patients during this period was 794, of whom 402 were still alive in 1941. In this year the number of diabetics was 3.8 per 1,000 of the population (3.2 per 1,000 for males and 4.3 per 1,000 for females). During the period covered by the study there was a steady rise in the incidence rate: in 1925 there were between 100 and 180 diabetics; in 1934 the figure had risen to between 300 and 350, whilst in 1940 it was 400. A comparison of the mortality among diabetic subjects with the general mortality in Norway gave the following figures: in the period 1925-1934 the mortality among male diabetics was 4·7 x the expected mortality rate, and among female diabetics it was 3·2 x the expected mortality. In the period 1934-1942 the corresponding figures were 2·7 and 2·3. This "excess mortality" for diabetics was greatest in the younger age-groups and decreased with age. Sixty cases of diabetic coma occurred during the period under investigation, and the mortality rate among these was 40 per cent.; these deaths represented 8·2 per cent. of all diabetic deaths. Hypertension was rare under the age of fifty; above this age a systolic pressure of over 160 mm. Hg was found in 43 per cent. of males and 68 per cent. of females, whilst a diastolic pressure of over 100 mm. Hg was found in 25 per cent. of males and in 36 per cent. of females. Among 104 diabetics examined during 1940-1941, there were 18 with diabetic retinitis. Pulmonary tuberculosis was responsible for 4·1 per cent. of the deaths among diabetics.

Ringworm of the Scalp

A SERIES of articles on the treatment of ringworm of the scalp (*Journal of the American Medical Association*, September 14, 1946, **132**, 58, 62, 65, 67) gives an evaluation, based upon the cure rate, of different methods of local therapy. L. Schwartz et al. obtained a cure rate of 84 per cent. by the use of salicylanilide ointment (salicylanilide 5 per cent. in carbowax 1,500). The selection of this medicament followed a comparative trial with a number of other local applications. A note attached by the Medical Officer of Washington County states that salicylanilide ointment is at present being used exclusively in the treatment of tinea capitis with highly satisfactory results, and that by this means the infection can be controlled without excluding the child from school during the period of treatment. G. M. Lewis *et al.*, following an estimation of the value of local endocrine therapy, record disappointing results with testosterone, œstradiol and diethylstilbœstrol, and advocate the use of X-ray therapy, a measure which resulted in their series in a cure rate of 90 per cent. The fungicides, including streptothricin (J. Lowry Miller *et al.*) proved disappointing, but a cure rate of 64 per cent. was obtained by A. Strickler, who used iodine enhanced by the application of photosynthesis. The mixture employed was: iodine 78 per cent., red blood cells 2 per cent., sodium chloride 1.9 per cent., chlorophyll (2 per cent. in isotonic solution of sodium chloride) 0.07 per cent., deceresol 10 per cent., magnesium dioxide 8 per cent., and spleen extract 0·005 per cent., incorporated in an oily vehicle, in the amount of 2 gm. of the mixture to 30 gm. oil (cottonseed oil). After clipping the hair, acetic acid is rubbed into the scalp by means of a toothbrush for two minutes; an electric bulb (150 to 200 watt) is then kept sufficiently close to the scalp to generate heat for two minutes, then the iodine and oil combination is rubbed in with friction, using another toothbrush, and heat is again applied locally for six minutes.

Contramine in the Treatment of Herpes Zoster

SATISFACTORY results from the use of contramine (diethyl - ammonium - diethyl · dithio - carbamate) in the treatment of sixteen patients with herpes zoster are reported by D. N. Bengis (*South African Medical Journal*, August 24, 1946, **20**, 467). The preparation was given intramuscularly in doses of 0.125 gm. per c.cm., one injection being given daily until pain had subsided, with a maximum of six injections. In most cases there was rapid relief of pain, the duration varying from one day (in one case) to seven days (in one case). The average number of injections required was three. In addition to alleviation of pain there was fairly rapid drying

of the vesicles. The response was more satisfactory in younger patients. In one patient, aged thirteen years, the administration of contramine was accompanied by slight nausea; in three, vesicles developed in spite of the administration of contramine, but in only one patient was there any post-herpetic neuralgia.

Vitamins in Pernicious Anæmia

As the result of an estimation of vitamin levels (A, B, and C) in eight patients with pernicious anæmia, using as controls twenty-five patients with known deficiency of the vitamin B complex and thirty normal medical students, D. Cayer *et al.* (*American Journal of Medical Sciences*, August 1946, **212**, 179) report that in the patients with pernicious anæmia there was no appreciable alteration in the level of vitamins A and C, but there was a definite decrease in the levels of nicotinic acid, thiamin and riboflavin. The figures for these three components of the B complex was practically the same as for the patients with known vitamin B deficiency. There was no correlation between the degree of anæmia and the vitamin levels in either group of patients. These findings, it is suggested, explain the healing of the oral lesions of pernicious anæmia which sometimes occurs with the administration of the vitamin B complex, and it is also suggested that these results "justify the administration of B complex vitamin to patients having pernicious anæmia if liver extract alone fails to produce a satisfactory response".

A Penicillin Injector

A RECOGNIZED disadvantage of penicillin therapy is the discomfort of the three-hourly injections, and particularly when prolonged treatment is necessary. A simple apparatus which obviates the discomfort and permits nocturnal injections without waking the patient is described by J. P. Baird and D. P. Jones (*Journal of the Royal Army Medical Corps*, August 1946, **87**, 91). The parts required are (1) a strong intramuscular hypodermic needle (5 c.cm. serum needle, 21 G x 1¾ inches); (2) a piece of stout-walled rubber tubing (size no. 12, bore 7/32 inch and wall 1/16 inch) 2 inches long; (3) a 2½ inch long piece of glass tubing (5.5 to 6 mm. diameter). The rubber tubing should fit the collar of the needle and plunger tightly so as to prevent leakage, but it must permit the plunger being moved up and down, as with a syringe. The apparatus is sterilized by boiling. The area of the injection site is shaved and sterilized and the needle thrust deeply into the muscle. Collodion is painted round the needle at its entrance through the skin and the apparatus is secured with a collar of adhesive tape. The plunger is pulled back about ½ an inch, an area of the tubing cleaned and the penicillin injected

through the tubing, using a syringe with a fine needle. (Care must be taken that the needle is inserted diagonally so that leakage may no occur after the tube has been punctured severa times.) The plunger is then pushed home: it is covered with a swab and strapping until the nex injection. So that the injected area may not be come too painful, and also to lessen the risk of sepsis, the injector and needle should be re moved and re-sterilized and the site of injectio changed every twenty-four hours. If a fairl wide area is shaved, removal of the swab an strapping can be carried out without disturbin a sleeping patient.

A New Method of Treatment c Pterygium

A NEW method of treatment of pterygium whic is stated to give highly satisfactory results bot from the surgical and the cosmetic points o view is described by S. Kamel (*British Journ of Ophthalmology*, September 1946, **30**, 549 The author divides the cases into two group (1) atrophic, in which the inflammatory proce: has subsided and regression with degenerati and atrophy has taken place, and (2) progressiv cases in which the inflammation is still activ The atrophic cases are either left as they at or are immediately operated on. In the progre: sive cases treatment with zinc sulphate drop ½ per cent., three to four times daily, and yello precipitate ointment, 1 per cent. twice daily, given for about ten to fifteen days. If there is an discharge, 10 per cent. argyrol drops are use but painting of the lids with silver nitrat which causes irritation, is avoided. Usually fou to five days' treatment proves sufficient, an the patient can then be operated on. Cocain 1 per cent. is instilled every two minutes, fiv to six drops being sufficient. The eye is the washed with bland antiseptic solution (subl mate 1:7000) and the speculum inserted. Th neck of the pterygium is caught with fixatio forceps and the head shaved from the corne attachment. The head of the pterygium is hel with fixation forceps and the pterygium we undermined up to the caruncle, when it i released with the eye directed forwards, car being taken to see that no part is left lyin

over the cornea. The fold of the conjunctiva will now return to its place. If, as in some long-standing cases, a small piece of the head of the pterygium is found to be still redundant, it must be excised with scissors with the gaze directed forwards, so that the edge of the pterygium butts against the limbus: the pterygium is then held with fixation forceps, the conjunctiva raised away from the sclera and the undersurface cauterized with carbolic acid, care being taken not to cauterize the surface of the sclera. No stitches are needed, but before bandaging the eye a piece of yellow-precipitate ointment 1 per cent. is put in the lower cul-de-sac. The eye is dressed daily for four or five days with zinc sulphate drops ½ per cent. and yellow precipitate ointment ½ per cent., after which the bandage is discarded. The zinc sulphate drops and yellow precipitate ointment are continued for another ten to twenty days. During the past six or seven years 600 cases have been treated by the author by this method, most of which have been periodically followed and observed, and not one single recurrence has been noted.

Streptomycin Therapy

A REPORT of the use of streptomycin in fifty-six patients with different types of surgical infection is given by J. W. Hirshfeld, C. W. Buggs, M. A. Pilling, B. Bronstein and C. H. O'Donnell (*Archives of Surgery*, April 1946, **52**, 387). It was found that streptomycin promptly sterilized the blood stream in bacteriæmia and septicæmia when the organisms involved were susceptible to its action, but even when such organisms were susceptible to streptomycin, sterilization of walled-off collections of pus was not obtained. In infections of the urinary tract, the high concentration in which streptomycin is excreted in the urine rendered it a valuable therapeutic agent when the organisms were susceptible to its action, but in peritonitis and infections of the soft tissues the results obtained were disappointing, no doubt owing to the presence of resistant organisms of which the most prominent group seemed to be the non-sporulating anærobes. Toxic reactions to streptomycin occurred in twelve of the fifty-six patients treated. A further contribution to the subject is contained in the results of a study of 1,000 cases of different infections carried out by fifty-five investigators accredited to the Committee on Chemotherapeutic and Other Agents of the National Research Council U.S.A.(*Journal of the American Medical Association*, September 7 and 14, 1946, **132**, 4 and 70). Streptomycin was found to be most effective in the treatment of tularæmia, *H. influenzæ* infections, urinary tract infections due to gram-negative bacilli, bac-

teriæmias, and meningitis due to gram-negative bacilli. Encouraging results were obtained in experimental and clinical peritonitis, which are stated to warrant more extensive clinical study. Seventy-five patients with different types of tuberculosis were among those studied and the results indicated that streptomycin was likely to prove valuable as a palliative remedy, although the experience gained did not indicate eradication of the infection.

Benadryl in the Treatment of Irradiation Sickness

PROMISING results are reported by J. E. Lofstrom and C. E. Nurnberger (*American Journal of Rœntgenology*, August 1946, **56**, 211) from the use of benadryl (beta-dimethylamino-ethyl benzhydryl ether hydrochloride) in the treatment of irradiation sickness. The drug was given either intravenously in doses of 50 to 100 mgm., or orally as capsules containing 50 mgm, one capsule being given four-hourly; the number of capsules required in a given case varied from 3 to 14. Nineteen patients were treated, but one defaulted during treatment; the remaining eighteen patients all improved and all but one were able to continue with their daily X-ray treatment without interruption. Not only were the sickness and nausea relieved, but there was also improvement in the mental condition of the patients. Although the most dramatic results were obtained from intravenous administration, it is these observers' impression that oral administration provides relief in the majority of cases. The rationale proposed for this beneficial action of benadryl is that the manifestations of irradiation sickness are due to the production of histamine by the irradiation, and that this histamine effect is counteracted by benadryl.

Brighter X-Ray Departments

A PLEA to make X-ray departments less terrifying to children is made by Elizabeth Boyle (*Radiography*, September 1946, **12**, 104). Her suggestions are to have "decorations in bright colours—pastel shades if you will, but anyway bright; also a nursery frieze half-way up the wall, illustrating well-loved nursery rhymes. Then multi-coloured circles on the ceiling and a revolving ball, or some similar moving mechanism, to absorb the child's attention so that she will be content to lie still after much time having been spent on positioning and centring". Black tube shields and fan-cooled tubes are particularly terrifying to children; the former should be brightly coloured and tubes should not be fan-cooled. Finally, "a few minutes spent in gaining the child's friendship by a few kind words before the ordeal saves a lot of wasted time on the table".

of the vesicles. The response was more satisfactory in younger patients. In one patient, aged thirteen years, the administration of contramine was accompanied by slight nausea; in three, vesicles developed in spite of the administration of contramine, but in only one patient was there any post-herpetic neuralgia.

Vitamins in Pernicious Anæmia

As the result of an estimation of vitamin levels (A, B, and C) in eight patients with pernicious anæmia, using as controls twenty-five patients with known deficiency of the vitamin B complex and thirty normal medical students, D. Cayer *et al.* (*American Journal of Medical Sciences*, August 1946, **212**, 179) report that in the patients with pernicious anæmia there was no appreciable alteration in the level of vitamins A and C, but there was a definite decrease in the levels of nicotinic acid, thiamin and riboflavin. The figures for these three components of the B complex was practically the same as for the patients with known vitamin B deficiency. There was no correlation between the degree of anæmia and the vitamin levels in either group of patients. These findings, it is suggested, explain the healing of the oral lesions of pernicious anæmia which sometimes occurs with the administration of the vitamin B complex, and it is also suggested that these results "justify the administration of B complex vitamin to patients having pernicious anæmia if liver extract alone fails to produce a satisfactory response".

A Penicillin Injector

A RECOGNIZED disadvantage of penicillin therapy is the discomfort of the three-hourly injections, and particularly when prolonged treatment is necessary. A simple apparatus which obviates the discomfort and permits nocturnal injections without waking the patient is described by J. P. Baird and D. P. Jones (*Journal of the Royal Army Medical Corps*, August 1946, **87**, 91). The parts required are (1) a strong intra-muscular hypodermic needle (5 c.cm. serum needle, 21 G x 1¾ inches); (2) a piece of stout-walled rubber tubing (size no. 12, bore 7/32 inch and wall 1/16 inch) 2 inches long; (3) a 2½ inch long piece of glass tubing (5.5 to 6 mm. diameter). The rubber tubing should fit the collar of the needle and plunger tightly so as to prevent leakage, but it must permit the plunger being moved up and down, as with a syringe. The apparatus is sterilized by boiling. The area of the injection site is shaved and sterilized and the needle thrust deeply into the muscle. Collodion is painted round the needle at its entrance through the skin and the apparatus is secured with a collar of adhesive tape. The plunger is pulled back about ½ an inch, an area of the tubing cleaned and the

through the tubing, using a syringe with a fine needle. (Care must be taken that the needle is inserted diagonally so that leakage may not
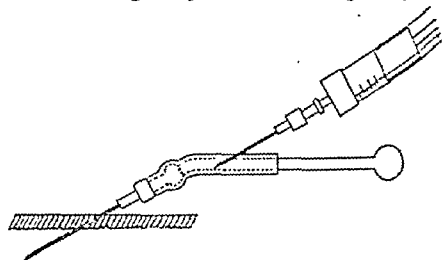
occur after the tube has been punctured several times.) The plunger is then pushed home: it is covered with a swab and strapping until the next injection. So that the injected area may not become too painful, and also to lessen the risk of sepsis, the injector and needle should be removed and re-sterilized and the site of injection changed every twenty-four hours. If a fairly wide area is shaved, removal of the swab and strapping can be carried out without disturbing a sleeping patient.

A New Method of Treatment of Pterygium

A NEW method of treatment of pterygium which is stated to give highly satisfactory results both from the surgical and the cosmetic points of view is described by S. Kamel (*British Journal of Ophthalmology*, September 1946, **30**, 549. The author divides the cases into two groups: (1) atrophic, in which the inflammatory process has subsided and regression with degeneration and atrophy has taken place, and (2) progressive cases in which the inflammation is still active. The atrophic cases are either left as they are or are immediately operated on. In the progressive cases treatment with zinc sulphate drops ½ per cent., three to four times daily, and yellow precipitate ointment, 1 per cent. twice daily, is given for about ten to fifteen days. If there is any discharge, 10 per cent. argyrol drops are used but painting of the lids with silver nitrate which causes irritation, is avoided. Usually four to five days' treatment proves sufficient, and the patient can then be operated on. Cocain 1 per cent. is instilled every two minutes, five to six drops being sufficient. The eye is then washed with bland antiseptic solution (sublimate 1:7000) and the speculum inserted. The neck of the pterygium is caught with fixation forceps and the head shaved from the cornea attachment. The head of the pterygium is held with fixation forceps and the pterygium well undermined up to the caruncle, when it is released with the eye directed forwards, care being taken to see that no part is left lying

phenomenal that even the expert tends to find himself out of date. This in turn involves the clinician, because even official regulations concerning the preparation and keeping properties of penicillin may be out of date almost before they are issued. As a guide to the present position this book could scarcely be improved upon. The various forms in which penicillin is provided for clinical use are subjected to critical review, and when there are good reasons for believing that even *B.P.* formulæ can be improved upon, these are carefully outlined and discussed. At times this spirit of criticism may be carried too far, as in the deprecation of precautions that have been recommended in the use of penicillin cream, but on the whole the criticisms and suggested modifications are usually fully justified. The practitioner who has mastered the contents of this book will have gone a long way towards ensuring that he is making the best possible use of this potent chemotherapeutic agent. It need only be added that the pharmacist will find it equally useful.

The Human Approach. BY HENRY YELLOWLEES, O.B.E., M.D., F.R.F.P.S., F.R.C.P., D.P.M. London: J. & A. Churchill, Ltd., 1946. Pp. vii and 189. Price 10s. 6d.

IT is a melancholy commentary on our times that a book should be valuable because it expounds a truism. But, especially now that individuality is wilting under mass direction, directors of medical studies and deans of medical schools would do well to read this book and reflect. Indeed, it would seem more important for them to do so than for the students to whom it is primarily addressed. It is because truths are dismissed so often as self-evident, that this book fills, as its author intends, a real defect in medical training. Whether it forms the best vehicle for its base is less certain, as the author in his preface seems to be aware. Metaphor, allegory, quotation, anecdote, discursiveness, pungency, pedantry and slanginess form a strange Scotch broth; but it is nourishing; in its "affective suggestion" it is not unappetizing; and it contains a vital ingredient usually missing from the menu of medical education.

Diabetes. BY HENRY J. JOHN, M.D., F.A.C.P. London: Henry Kimpton, 1946. Pp. 300. Charts 73. Price 17s.

THIS is a curiously uneven book. The author belongs to the school that believes that hyperglycæmia plays a vital rôle in diabetes mellitus by "doing damage to the islands of Langerhans and in time destroying them". The result is that he insists upon the control of the condition by frequent blood sugar estimations. Glycosuria he considers of little value in diagnosis and controlling treatment. This is a view that has never been generally accepted in this country, and when in advocating his view the author makes statements such as "there is no such thing as a 'normal renal threshold' ", the book is scarcely one that can be recommended to practitioners in Great Britain. On the other hand, there is much sound teaching, as in the author's advocacy of the view that diets must be made as liberal as possible, especially in children. The chapter on pregnancy and diabetes would have been improved by more adequate discussion of the difficult problem of treatment. A surprising innovation is a chapter on the salivary glands and their possible rôle in diabetes mellitus. The expert will find much of interest in this book, but it is not one to commend to the novice or the practitioner who only sees an occasional case of diabetes mellitus.

NEW EDITIONS

Gray's Anatomy, edited by T. B. JOHNSTON, C.B.E., M.D., and J. WHILLIS, M.D., M.S., in its twenty-ninth edition (Longmans, Green and Co., 70s.) has been extensively revised and rewritten, and particularly in the section dealing with the development of the human embryo and the chapter on neurology. Nearly two hundred new figures have been included, among them a number of X-ray plates, bringing the total up to 1,359. Some of the illustrations are coloured, and all are beautifully produced.

IN the ninth edition of *The Diabetic A B C*, by R. D. LAWRENCE, M.D., F.R.C.P. (H. K. Lewis and Co., Ltd., 4s.) the hope expressed by the author in the previous edition that the wartime supplement might be omitted has been fulfilled. In view of the continued restricted diet, however, a post-war diet section has been added, which will be welcomed by all diabetics and their medical advisers.

Skin Diseases in Children, by GEORGE M. MACKEE, M.D., and ANTHONY C. CIPOLLARO, M.D., in its second edition (Hamish Hamilton Medical Books, 37s. 6d.) has been brought up to date in all sections. Not only is the work richly illustrated, containing in all 225 figures which greatly aid diagnosis, but each chapter concludes with a most useful bibliography. The work is beautifully produced, and both authors and publishers are to be congratulated on the production of this welcome new edition.

A Synopsis of Surgical Anatomy, by ALEXANDER LEE McGREGOR, M.CH., F.R.C.S. (John Wright & Sons, Ltd., 25s.), in its sixth edition, has been brought up to date in accordance with modern developments. The section on Volkman's contracture has been rewritten.

REVIEWS OF BOOKS

The Hunterian Museum: Yesterday and Tomorrow. BY PROFESSOR G. GREY TURNER, M.S., F.R.C.S. London: Cassell and Company Ltd., 1946. Pp. viii and 87. Figures 41. Price 15s.

PROFESSOR GREY TURNER has expanded his Hunterian oration of 1945 into a book of eighty pages, profusely illustrated. In it he deals with the life and times of Hunter, the origin of museums and the place they fill in teaching and research, the beginnings and growth of Hunter's own collection, its fate after his death, and its expansion under a succession of men who shared his ideals, until in its heyday it was by a wide margin the most valuable collection in the world. He speaks of the disaster of 1941, of the labours that have reassembled what was left and that are now being directed to make the museum once more the leading centre of surgical research, and of the future lines on which it should develop. The charm of this delightful book lies in its discursive style which passes in turn from Hunter to the museum and back to Hunter again, from Hunter to the fields and woods and back to the museum, from Hunter's experiments and specimens to the author's own experiences in a long life of surgical work to which he has brought an outlook that is in many ways Hunterian. Grey Turner has always been a collector, a thinker and a reader, and his many writings and his ever welcome contributions to discussions have been valued because of their uniformily personal touch. Every surgeon will treasure this small book for what it tells of Hunter, of the history of the college, and of the writer himself.

Child and Adolescent Life in Health and Disease. BY W. S. CRAIG, B.Sc., M.D., F.R.C.P.E., F.R.S.Ed. Foreword by PROFESSOR CHARLES MCNEIL, M.D., F.R.C.P., F.R.C.P.E., F.R.S.Ed. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. 667. Figures 202. Price 25s.

THIS handsomely produced volume is a typical product of the Edinburgh School of Medicine —comprehensive, thorough and accurate. As "a study in social pædiatrics", to give it its sub-title, it is an outstanding contribution to an aspect of medicine which of recent years has come rapidly to the fore. Social medicine, in spite of the claims of some of its more enthusiastic advocates, is no new phenomenon—for generations the family practitioner has been fully aware of the impact of environment upon the health of his patients. What is happening to-day

is an organized development by the State of social welfare commensurate with the increasing complexity of modern life. One inevitable, if temporary, result of this intervention of the State is a tendency to overlapping between voluntary, municipal and government schemes, with the result that both the medical practitioner and the social welfare worker tend to find the present situation confusing and apparently lacking in coordination. At this particular stage in our social history, when a historic Education Act has just reached the statute book and an equally historic National Health Bill is about to become law, a summary of our social services is particularly welcome and in providing such a survey Professor Craig has placed medical practitioners and social workers alike in his debt. Not only does he trace the development of social pædiatrics from the twelfth century to the present day, but he also discusses fully the various schemes that are now in force for the care of the child: the problem of the homeless child, the juvenile in need of care and protection, the handicapped child and the sick child. In addition, legislation relating to child and adolescent welfare is fully outlined and there is a most useful series of appendices giving details of hospitals, institutions and societies which cater for the welfare of the child. Profusely illustrated with a series of brilliant photographs illustrating all aspects of the subject, this book can well be described as an essential component of the library of all who are interested in the welfare of children. It will for long be the standard work on the subject in this country.

Penicillin: Its Properties, Uses and Preparations. Published by direction of the Council of The Pharmaceutical Society of Great Britain. London: The Pharmaceutical Press, 1946. Pp. viii and 199. Illustrated. Price 10s. 6d.

THIS is an excellent addition to the growing number of books on penicillin. Its two outstanding merits are that, written by experts, provides a critical review of the present status of the antibiotic, and at the same time it provides the medical practitioner with a clear account of the pharmaceutical problems associated with the manufacture, assay and prescribing of penicillin. This latter merit is particularly important because unless the practitioner appreciates the problems involved it is not possible for him to use the preparation to the best advantage of the patient. The advances in the knowledge of penicillin have been so

phenomenal that even the expert tends to find himself out of date. This in turn involves the clinician, because even official regulations concerning the preparation and keeping properties of penicillin may be out of date almost before they are issued. As a guide to the present position this book could scarcely be improved upon. The various forms in which penicillin is provided for clinical use are subjected to critical review, and when there are good reasons for believing that even *B.P.* formulæ can be improved upon, these are carefully outlined and discussed. At times this spirit of criticism may be carried too far, as in the deprecation of precautions that have been recommended in the use of penicillin cream, but on the whole the criticisms and suggested modifications are usually fully justified. The practitioner who has mastered the contents of this book will have gone a long way towards ensuring that he is making the best possible use of this potent chemotherapeutic agent. It need only be added that the pharmacist will find it equally useful.

The Human Approach. By HENRY YELLOWLEES, O.B.E., M.D., F.R.F.P.S., F.R.C.P., D.P.M. London: J. & A. Churchill, Ltd., 1946. Pp. vii and 189. Price 10s. 6d.

IT is a melancholy commentary on our times that a book should be valuable because it expounds a truism. But especially now that individuality is wilting under mass direction, directors of medical studies and deans of medical schools would do well to read this book and reflect. Indeed, it would seem more important for them to do so than for the students to whom it is primarily addressed. It is because truths are dismissed so often as self-evident, that this book fills, as its author intends, a real defect in medical training. Whether it forms the best vehicle for its base is less certain, as the author in his preface seems to be aware. Metaphor, allegory, quotation, anecdote, discursiveness, pungency, pedantry and slanginess form a strange Scotch broth; but it is nourishing; in its "affective suggestion" it is not unappetizing; and it contains a vital ingredient usually missing from the menu of medical education.

Diabetes. By HENRY J. JOHN, M.D., F.A.C.P. London: Henry Kimpton, 1946. Pp. 300. Charts 73. Price 17s.

THIS is a curiously uneven book. The author belongs to the school that believes that hyperglycæmia plays a vital rôle in diabetes mellitus by "doing damage to the islands of Langerhans and in time destroying them". The result is that he insists upon the control of the condition by frequent blood sugar estimations. Glycosuria

he considers of little value in diagnosis and controlling treatment. This is a view that has never been generally accepted in this country, and when in advocating his view the author makes statements such as "there is no such thing as a 'normal renal threshold'", the book is scarcely one that can be recommended to practitioners in Great Britain. On the other hand, there is much sound teaching, as in the author's advocacy of the view that diets must be made as liberal as possible, especially in children. The chapter on pregnancy and diabetes would have been improved by more adequate discussion of the difficult problem of treatment. A surprising innovation is a chapter on the salivary glands and their possible rôle in diabetes mellitus. The expert will find much of interest in this book, but it is not one to commend to the novice or the practitioner who only sees an occasional case of diabetes mellitus.

NEW EDITIONS

Gray's Anatomy, edited by T. B. JOHNSTON, C.B.E., M.D., and J. WHILLIS, M.D., M.S., in its twenty-ninth edition (Longmans, Green and Co., 70s.) has been extensively revised and rewritten, and particularly in the section dealing with the development of the human embryo and the chapter on neurology. Nearly two hundred new figures have been included, among them a number of X-ray plates, bringing the total up to 1,359. Some of the illustrations are coloured, and all are beautifully produced.

IN the ninth edition of *The Diabetic A B C*, by R. D. LAWRENCE, M.D., F.R.C.P. (H. K. Lewis and Co., Ltd., 4s.) the hope expressed by the author in the previous edition that the wartime supplement might be omitted has been fulfilled. In view of the continued restricted diet, however, a post-war diet section has been added, which will be welcomed by all diabetics and their medical advisers.

Skin Diseases in Children, by GEORGE M. MACKEE, M.D., and ANTHONY C. CIPOLLARO, M.D., in its second edition (Hamish Hamilton Medical Books, 37s. 6d.) has been brought up to date in all sections. Not only is the work richly illustrated, containing in all 225 figures which greatly aid diagnosis, but each chapter concludes with a most useful bibliography. The work is beautifully produced, and both authors and publishers are to be congratulated on the production of this welcome new edition.

A Synopsis of Surgical Anatomy, by ALEXANDER LEE McGREGOR, M.CH., F.R.C.S. (John Wright & Sons, Ltd., 25s.), in its sixth edition, has been brought up to date in accordance with modern developments. The section on Volkman's contracture has been rewritten.

REVIEWS OF BOOKS

The Hunterian Museum: Yesterday and Tomorrow. BY PROFESSOR G. GREY TURNER, M.S., F.R.C.S. London: Cassell and Company Ltd., 1946. Pp. viii and 87. Figures 41. Price 15s.

PROFESSOR GREY TURNER has expanded his Hunterian oration of 1945 into a book of eighty pages, profusely illustrated. In it he deals with the life and times of Hunter, the origin of museums and the place they fill in teaching and research, the beginnings and growth of Hunter's own collection, its fate after his death, and its expansion under a succession of men who shared his ideals, until in its heyday it was by a wide margin the most valuable collection in the world. He speaks of the disaster of 1941, of the labours that have reassembled what was left and that are now being directed to make the museum once more the leading centre of surgical research, and of the future lines on which it should develop. The charm of this delightful book lies in its discursive style which passes in turn from Hunter to the museum and back to Hunter again, from Hunter to the fields and woods and back to the museum, from Hunter's experiments and specimens to the author's own experiences in a long life of surgical work to which he has brought an outlook that is in many ways Hunterian. Grey Turner has always been a collector, a thinker and a reader, and his many writings and his ever welcome contributions to discussions have been valued because of their uniformily personal touch. Every surgeon will treasure this small book for what it tells of Hunter, of the history of the college, and of the writer himself.

Child and Adolescent Life in Health and Disease. BY W. S. CRAIG, B.Sc., M.D., F.R.C.P.E., F.R.S.ED. Foreword by PROFESSOR CHARLES MCNEIL, M.D., F.R.C.P., F.R.C.P.E., F.R.S.ED. Edinburgh: E. & S. Livingstone Ltd., 1946. Pp. 667. Figures 202. Price 25s.

THIS handsomely produced volume is a typical product of the Edinburgh School of Medicine —comprehensive, thorough and accurate. As "a study in social pædiatrics", to give it its subtitle, it is an outstanding contribution to an aspect of medicine which of recent years has come rapidly to the fore. Social medicine, in spite of the claims of some of its more enthusiastic advocates, is no new phenomenon—for generations the family practitioner has been fully aware of the impact of environment upon the health of his patients. What is happening to-day

is an organized development by the State of social welfare commensurate with the increasing complexity of modern life. One inevitable, if temporary, result of this intervention of the State is a tendency to overlapping between voluntary, municipal and governmental schemes, with the result that both the medical practitioner and the social welfare worker tend to find the present situation confusing and apparently lacking in coordination. At this particular stage in our social history, when an historic Education Act has just reached the statute book and an equally historic National Health Bill is about to become law, a summary of our social services is particularly welcome, and in providing such a survey Professor Craig has placed medical practitioners and social workers alike in his debt. Not only does he trace the development of social pædiatrics from the twelfth century to the present day, but he also discusses fully the various schemes that are now in force for the care of the child: the problem of the homeless child, the juvenile in need of care and protection, the handicapped child and the sick child. In addition, legislation relating to child and adolescent welfare, is fully outlined, and there is a most useful series of appendices giving details of hospitals, institutions and societies which cater for the welfare of the child. Profusely illustrated with a series of brilliant photographs illustrating all aspects of the subject, this book can well be described as an essential component of the library of all who are interested in the welfare of children. It will for long be the standard work on the subject in this country.

Penicillin: Its Properties, Uses and Preparations. Published by direction of the Council of The Pharmaceutical Society of Great Britain. London: The Pharmaceutical Press, 1946. Pp. viii and 199. Illustrated. Price 10s. 6d.

THIS is an excellent addition to the growing number of books on penicillin. Its two outstanding merits are that, written by experts, it provides a critical review of the present status of the antibiotic, and at the same time it provides the medical practitioner with a clear account of the pharmaceutical problems associated with the manufacture, assay and prescribing of penicillin. This latter merit is particularly important because unless the practitioner appreciates the problems involved it is not possible for him to use the preparation to the best advantage of the patient. The advances in the knowledge of penicillin have been so

THE
PRACTITIONER

Edited by

SIR HENEAGE OGILVIE
K.B.E., D.M., M.CH., F.R.C.S.

and

WILLIAM A. R. THOMSON
M.D.

JULY—DECEMBER 1946

THE PRACTITIONER
5 BENTINCK STREET, LONDON, W.1

1 9 4 6

NOTES AND PREPARATIONS

NUFFIELD FOUNDATION: RESEARCH IN CHRONIC RHEUMATISM

WITH the assistance of a grant of £100,000 spread over 10 years, from the Nuffield Foundation, a rheumatism centre is to be established at Manchester University, comprising a diagnosis and teaching centre at the Manchester Royal Infirmary for short-stay and out-patients, and clinics at a nearby base hospital and also at the Devonshire Royal Hospital, Buxton, for the treatment of long-stay patients. The etiological, clinical, sociological and industrial aspects of the disease will be studied. It is pointed out that an important element in the organization will be the diffusion throughout the area of expert knowledge gained at the University centre, a diffusion which will ultimately be widened by the better knowledge of the subject of rheumatism obtained by students at the Medical School of the University.

THE CENTENARY OF ANÆSTHESIA

DURING the past few weeks the centenary of the practical introduction of anæsthesia has been celebrated here and in the United States. On October 31, the President and Council of the Royal College of Surgeons held a reception in the College, at which a plaque erected by the Association of Anæsthetists was unveiled by H.R.H. the Princess Royal. Before the unveiling ceremony a short lecture was given by Dr. A. D. Marston, President of the Association of Anæsthetists. On October 16, the Section of the History of Medicine of the Royal Society of Medicine held a special meeting, which was followed by a visit to an exhibition of anæsthetic apparatus and literature at the Wellcome Historical Medical Museum, opened by Lord Moran, President of the Royal College of Physicians. The Association of Anæsthetists gave a centenary dinner in the Great Hall of Lincoln's Inn on October 31, and on November 1, the Anæsthetic Section of the Royal Society of Medicine held a reception, after which a Presidential address on 'A Hundred Years of Anæsthesia' was delivered by Dr. E. S. Rowbotham.

THE R.N.V.R. CLUB

Lieut. the Hon. W. W. Astor, R.N.V.R., Chairman of the R.N.V.R. Club, writes:—

"During the war no less than 2,700 doctors held commissions in the R.N.V.R. They served with great distinction in all classes of ships and in all parts of the world. Many lost their lives. It may therefore interest members of the medical profession to know that the R N V R Officers' Commemoration Fund has been opened to commemorate in a practical way the part R N V R. Officers played in the war, and in particular those who lost their lives. The Fund has two objects, (1) to purchase and equip the new premises of the R.N.V.R. Club, and (2) to start an adequate Welfare Fund to help R.N.V R. Officers and their dependants who may stand in need

The new Club will have a memorial tablet, and relative of officers who were killed may through this Fund have Officers' names inscribed on it. This Club was started during the war, and has grown from nothing to an institution with 10,000 members, and it provides good and cheap meals, accommodation and amenities, particularly for junior officers. But it must leave its wartime premises and without help it cannot get into new premises. The administration of the Welfare Fund is closely integrated with that of King George's Fund for Sailors.

We sincerely hope that many members of the medical profession, so many of whom served in the R.N.V.R will give their support. The money is urgently needed R.N.V.R. Officers themselves have generously supported the Fund, but most of them are young, and it is hoped that the outstanding part that they played in the war (when they formed 80 per cent. of the officer strength of the Navy) will commend this Appeal favourably to their fellow countrymen."

Cheques should be sent to Commodore Earl Howe, President of the R.N.V.R. Club, 52 Pall Mall, London, S.W.1.

TUBERCULOSIS IN THE WEST INDIES

A REPORT on the sociological and clinical survey of tuberculosis in the West Indies, written by W. Santon Gilmour, M.B., has been published by the National Association for the Prevention of Tuberculosis. The investigations were carried out during the period 1943-44. The incidence and mortality rate for tuberculosis is high in the West Indies: in 1943 the number of deaths from tuberculosis in Trinidad and Tobago was 100 per 100,000; in Barbados in 1942, 69 per 100,000; in Grenada during the years 1938-42, 79 per 100,000; and in the Bahamas in 1943 tuberculosis accounted for approximately one in every six deaths recorded. Apart from education and nutrition, housing is one of the chief causal factors, the type of house inhabited by most people being ideal for transmission of infection.

OFFICIAL NOTICES

You and Your Children, a collection of B.B.C. talks by a woman psychologist, is published by the Ministry of Health (H.M. Stationery Office price 6d.). The booklet is charmingly illustrated and deals with such problems as fear of the dark, habit training, and general problems in the child's upbringing, with hints for both fathers and mothers. *Priority Supplies of Milk to Invalids.* Owing to the scarcity of milk at this time of year and the increased demands on supply the Minister of Food has asked the medical profession to check up on the issue of certificates for priority milk: after November 30, 1946, no certificate dated before November 3, 1946, will be valid.

The contents for the January issue, which will contain a symposium on "The Acute Abdomen" and also the first article of a new series entitled "The Problems of Pain", will be found on page lxx at the end of the advertisement section.
Binding cases for volume 157 (July—December 1946), in green cloth with gilt lettering, are now ready, price 3s. od. post free, from *The Practitioner*, 5 Bentinck Street London, W.1.

GENERAL INDEX

TO VOLUME 157

SYMPOSIA

.

INDEX TO NAMES OF AUTHORS

GENERAL INDEX

TO VOLUME 157

SYMPOSIA

INDEX TO NAMES OF AUTHORS

INDEX TO SUBJECTS

Abbreviations: *abs* — Abstract; *NQ* — Note and Query; *RC* — Revision Corner

PREPARATIONS, ETC.